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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended March 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission file number: 001-36485

ARDELYX, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**26-1303944**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No)

34175 Ardenwood Boulevard, Fremont, California 94555
400 Fifth Avenue, Suite 210, Waltham, Massachusetts 02451
(Address of Principal Executive Offices) (Zip Code)

(510) 745-1700
(Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.0001	ARDX	The Nasdaq Global Market

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The number of issued and outstanding shares of the registrant's Common Stock, $0.0001 par value per share, as of May 3, 2021, was 98,709,188.

ARDELYX, INC.

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

ARDELYX, INC.
CONDENSED BALANCE SHEETS
(Unaudited)
(in thousands, except share and per share amounts)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 84,070	$ 91,032
Short-term investments	94,142	95,452
Accounts receivable	5,783	—
Prepaid expenses and other current assets	21,381	8,202
Total current assets	205,376	194,686
Property and equipment, net	2,292	1,936
Long-term investments	—	2,114
Right-of-use assets, net	1,667	2,274
Other assets	958	552
Total assets	$ 210,293	$ 201,562
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,378	$ 5,626
Accrued compensation and benefits	4,348	5,672
Current portion of operating lease liability	1,412	2,117
Loan payable, current portion	16,667	4,167
Deferred revenue	2,723	4,177
Accrued expenses and other current liabilities	11,262	6,657
Total current liabilities	41,790	28,416
Operating lease liability, net of current portion	397	413
Loan payable, net of current portion	34,348	46,621
Deferred revenue, non-current	2,947	—
Total liabilities	79,482	75,450
Commitments and contingencies (Note 11)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized; no shares issued and outstanding as of March 31, 2021 and December 31, 2020, respectively.	—	—
Common stock, $0.0001 par value; 300,000,000 shares authorized; 98,688,577 and 93,599,975 shares issued and outstanding as of March 31, 2021 and December 31, 2020, respectively.	10	9
Additional paid-in capital	718,728	680,872
Accumulated deficit	(587,920)	(554,765)
Accumulated other comprehensive income	(7)	(4)
Total stockholders' equity	130,811	126,112
Total liabilities and stockholders' equity	$ 210,293	$ 201,562

The accompanying notes are an integral part of these condensed financial statements.

ARDELYX, INC.
CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(Unaudited)
(in thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2021	2020
Revenues:		
Collaborative development revenue	$ 1,454	$ 1,175
Product supply revenue	126	38
Licensing revenue	5,002	—
Total revenues	6,582	1,213
Operating expenses:		
Cost of revenue	1,000	—
Research and development	20,456	15,844
General and administrative	17,131	7,138
Total operating expenses	38,587	22,982
Loss from operations	(32,005)	(21,769)
Interest expense	(1,100)	(1,357)
Other income (expense), net	(49)	753
Loss before provision for income taxes	(33,154)	(22,373)
Provision for income taxes	1	—
Net loss	$ (33,155)	$ (22,373)
Net loss per common share, basic and diluted	$ (0.34)	$ (0.25)
Shares used in computing net loss per share - basic and diluted	97,179,241	88,880,658
Comprehensive loss:		
Net loss	$ (33,155)	$ (22,373)
Unrealized (losses) gains on available-for-sale securities	(3)	(64)
Comprehensive loss	$ (33,158)	$ (22,437)

The accompanying notes are an integral part of these condensed financial statements.

ARDELYX, INC.
CONDENSED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY
For the Three Months ended March 31, 2021 and 2020
(Unaudited)
(in thousands, except shares)

	Three Months Ended March 31, 2021					
	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity
	Shares	Amount				
Balance as of December 31, 2020	93,599,975	$ 9	$ 680,872	$ (554,765)	$ (4)	$ 126,112
Issuance of common stock under employee stock purchase plan	102,208	—	478	—	—	478
Issuance of common stock upon exercise of options	10,507	—	20	—	—	20
Issuance of common stock upon vesting of restricted stock units	35,100	—	—	—	—	—
Issuance of common stock in at-the-market offering	4,940,787	1	34,271			34,272
Stock-based compensation	—	—	3,087	—	—	3,087
Unrealized losses on available-for-sale securities	—	—	—	—	(3)	(3)
Net loss	—	—	—	(33,155)	—	(33,155)
Balance as of March 31, 2021	98,688,577	$ 10	$ 718,728	$ (587,920)	$ (7)	$ 130,811

	Three Months Ended March 31, 2020					
	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity
	Shares	Amount				
Balance as of December 31, 2019	88,817,741	$ 9	$ 647,078	$ (460,452)	$ 20	$ 186,655
Issuance of common stock under employee stock purchase plan	75,804	—	375	—	—	375
Issuance of common stock upon exercise of options	141,551	—	216	—	—	216
Stock-based compensation	—	—	2,948	—	—	2,948
Unrealized gains on available-for-sale securities	—	—	—	—	(64)	(64)
Net loss	—	—	—	(22,373)	—	(22,373)
Balance as of March 31, 2020	89,035,096	$ 9	$ 650,617	$ (482,825)	$ (44)	$ 167,757

The accompanying notes are an integral part of these condensed financial statements.

ARDELYX, INC.
CONDENSED STATEMENTS OF CASH FLOWS
(Unaudited)
(in thousands)

	Three Months Ended March 31,	
	2021	**2020**
Operating activities		
Net loss	$ (33,155)	$ (22,373)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	422	492
Amortization of deferred financing costs	157	112
Amortization of deferred compensation for services	77	89
Amortization of (discount) premium on investment securities	157	(138)
Non-cash lease expense	607	502
Stock-based compensation	3,087	2,948
Change in derivative liabilities	36	82
Non-cash interest associated with debt discount accretion	70	127
Changes in operating assets and liabilities:		
Accounts receivable	(5,783)	—
Prepaid expenses and other assets	(13,662)	(928)
Accounts payable	(248)	(1,174)
Accrued compensation and benefits	(1,324)	(2,502)
Operating lease liabilities	(721)	(614)
Accrued and other liabilities	7,517	(394)
Deferred revenue	(1,454)	(1,175)
Net cash used in operating activities	(44,217)	(24,946)
Investing activities		
Proceeds from maturities and redemptions of investments	35,370	4,000
Purchases of investments	(32,107)	(54,858)
Purchases of property and equipment	(778)	(25)
Net cash provided by (used in) investing activities	2,485	(50,883)
Financing activities		
Proceeds from issuance of common stock in at-the-market offering, net of issuance costs	34,272	—
Proceeds from issuance of common stock under equity incentive and stock purchase plans	498	591
Net cash provided by financing activities	34,770	591
Net decrease in cash and cash equivalents	(6,962)	(75,238)
Cash and cash equivalents at beginning of period	91,032	181,133
Cash and cash equivalents at end of period	$ 84,070	$ 105,895
Supplementary disclosure of cash flow information:		
Cash paid for interest	$ 963	$ 1,142
Cash paid for income taxes	$ —	$ 2
Supplementary disclosure of non-cash activities:		
Right-of-use assets obtained in exchange for lease obligations	$ 450	$ 5,810

The accompanying notes are an integral part of these condensed financial statements.

ARDELYX, INC.
NOTES TO CONDENSED FINANCIAL STATEMENTS
(Unaudited)
(amounts in thousands, except per share amounts and where otherwise noted)

NOTE 1. ORGANIZATION AND BASIS OF PRESENTATION

Ardelyx, Inc. (the "Company," "we," "us" or "our") is a specialized biopharmaceutical company focused on discovering, developing and commercializing innovative first-in-class medicines to enhance the lives of patients with kidney and cardiorenal diseases.

We operate in one business segment, which is the research, development and commercialization of biopharmaceutical products.

Basis of Presentation

These condensed financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") and pursuant to the requirements of the Securities and Exchange Commission ("SEC") for interim reporting. As permitted under those rules and regulations, certain footnotes or other financial information that are normally required by U.S. GAAP have been condensed or omitted. These condensed financial statements have been prepared on the same basis as our most recent annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments necessary to present fairly our financial position at March 31, 2021 and results of operations, changes in stockholders' equity, and cash flows for the interim periods ended March 31, 2021 and 2020.

The accompanying condensed financial statements and related financial information should be read in conjunction with the audited financial statements and the related notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2020. The results for the three months ended March 31, 2021 are not necessarily indicative of results to be expected for the entire year ending December 31, 2021, or for any other interim period or future year.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and judgments that affect the amounts reported in the financial statements and accompanying notes thereto. On an ongoing basis, management evaluates its estimates, including those related to recognition of revenue, clinical trial accruals, contract manufacturing accruals, the fair value of assets and liabilities, income taxes and stock-based compensation. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could materially differ from those estimates.

Liquidity

As of March 31, 2021, we had cash, cash equivalents and marketable securities of approximately $178.2 million. We believe our current available cash, cash equivalents marketable securities will be sufficient to fund our planned expenditures and meet our obligations for at least 12 months following the filing of this Report on Form 10-Q. Failure to generate product revenue in a timely manner, or raise sufficient capital when needed, could have a negative impact on our financial condition and our ability to pursue our business strategies and could require us to significantly delay, scale back or discontinue one or more of our product development programs, commercialization efforts, or other aspects of our business plans, and our operating results and financial condition would be adversely affected.

Summary of Significant Accounting Policies

There have been no changes to the significant accounting policies disclosed in our most recent Annual Report on Form 10-K.

Recent Accounting Pronouncements

New Accounting Pronouncements - Recently Adopted

We have adopted no new accounting pronouncements other than those disclosed in our most recent Annual Report on Form 10-K.

Recent Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, an amendment which modifies the measurement and recognition of credit losses for most financial assets and certain other instruments. The amendment updates the guidance for measuring and recording credit losses on financial assets measured at amortized cost by replacing the "incurred loss" model with an "expected loss" model. Accordingly, these financial assets will be presented at the net amount expected to be collected. The amendment also requires that credit losses related to available-for-sale debt securities be recorded as an allowance through net income rather than reducing the carrying amount under the current, other-than-temporary-impairment model. For smaller reporting companies the guidance is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted. Management is currently assessing the impact of this standard on our financial statements.

NOTE 2. CASH, CASH EQUIVALENTS AND SHORT-TERM INVESTMENTS

Securities classified as cash, cash equivalents and short-term investments as of March 31, 2021 and December 31, 2020 are summarized below (in thousands):

	March 31, 2021			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 2,751	$ —	$ —	$ 2,751
Money market funds	76,676	—	—	76,676
Commercial paper	3,500	—	—	3,500
Corporate bonds	1,143	—	—	1,143
Total cash and cash equivalents	84,070	—	—	84,070
Short-term investments				
Commercial paper	$ 73,542	$ 3	$ (4)	$ 73,541
Corporate bonds	15,308	—	(6)	15,302
U.S. government-sponsored agency bonds	3,264	—	—	3,264
Asset-backed securities	2,035	—	—	2,035
Total short-term investments	94,149	3	(10)	94,142
Total cash equivalents and short-term investments	$ 178,219	$ 3	$ (10)	$ 178,212

	December 31, 2020			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 781	$ —	$ —	$ 781
Money market funds	88,151	—	—	88,151
Commercial paper	2,100	—	—	2,100
Total cash and cash equivalents	91,032	—	—	91,032
Short-term investments				
Commercial paper	$ 60,631	$ 2	$ (4)	$ 60,629
Corporate bonds	24,547	3	(6)	24,544
U.S. government-sponsored agency bonds	9,277	2	—	9,279
U.S. treasury notes	1,000	—	—	1,000
Total short-term investments	95,455	7	(10)	95,452
Long-term investments:				
Corporate bonds	$ 2,115		$ (1)	2,114
Total cash equivalents and short-term investments	$ 188,602	$ 7	$ (11)	$ 188,598

We invest excess cash in marketable securities with high credit ratings. These securities consist primarily of money market funds, commercial paper, corporate bonds, asset-backed securities, and U.S. treasury and agency securities and are classified as “available-for-sale.”

All available-for-sale securities held as of March 31, 2021 had contractual maturities of less than one year. Our available-for-sale securities are subject to a periodic impairment review. We consider a debt security to be impaired when the fair value of that security is less than its carrying cost, in which case we would further evaluate the investment to determine whether the security is other-than-temporarily impaired. When we evaluate an investment for other-than-temporary impairment, we review factors such as the length of time and extent to which fair value has been below cost basis, the financial condition or creditworthiness of the issuer and any changes thereto, intent to sell, and whether it is more likely than not we will be required to sell the investment before the recovery of its cost basis. If an investment is other-than-temporarily impaired, we write the investment down through the statement of operations to its fair value and establishes that value as the new cost basis for the investment. Management has determined that none of our available-for-sale securities were other-than-temporarily impaired in any of the periods presented, and as of March 31, 2021, no investment was in a continuous unrealized loss position for more than one year. As such, we believe that it is more likely than not that the investments will be held until maturity or a forecasted recovery of fair value.

NOTE 3. FAIR VALUE MEASUREMENTS

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs.

The three-level hierarchy for the inputs to valuation techniques is briefly summarized as follows:

Level 1 – Valuations are based on quoted prices in active markets for identical assets or liabilities and readily accessible by us at the reporting date. Examples of assets and liabilities utilizing Level 1 inputs are certain money market funds, U.S. treasuries and trading securities with quoted prices on active markets.

Level 2 – Valuations based on inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities. Examples of assets and liabilities utilizing Level 1 inputs are certain money market funds, U.S. treasuries and trading securities with quoted prices on active markets.

Level 3 – Valuations based on unobservable inputs for which there is little or no market data, which require us to develop our own assumptions.

The following table sets forth the fair value of our financial assets and liabilities that are measured or disclosed on a recurring basis by level within the fair value hierarchy (in thousands):

	March 31, 2021			
	Total Fair Value	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 76,676	$ 76,676	$ —	$ —
Commercial paper	77,041	—	77,041	—
Corporate bonds	16,445	—	16,445	—
U.S. government-sponsored agency bonds	3,264	—	3,264	—
Asset-backed securities	2,035	—	2,035	—
Total	$ 175,461	$ 76,676	$ 98,785	$ —
Liabilities:				
Derivative liability for Exit Fee	$ 1,412	$ —	$ —	$ 1,412
Total	$ 1,412	$ —	$ —	$ 1,412

	December 31, 2020			
	Total Fair Value	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 88,151	$ 88,151	$ —	$ —
Commercial paper	62,729	—	62,729	—
Corporate bonds	26,658	—	26,658	—
U.S. government-sponsored agency bonds	9,279	—	9,279	—
U.S. treasury notes	1,000	—	1,000	—
Total	$ 187,817	$ 88,151	$ 99,666	$ —
Liabilities:				
Derivative liability for Exit Fee	$ 1,376	$ —	$ —	$ 1,376
Total	$ 1,376	$ —	$ —	$ 1,376

Where quoted prices are available in an active market, securities are classified as Level 1. We classify money market funds as Level 1. When quoted market prices are not available for the specific security, we estimate fair value by using benchmark yields, reported trades, broker/dealer quotes and issuer spreads. We classify U.S. government-sponsored agency bonds, U.S. treasury notes, corporate bonds, commercial paper, asset-backed securities and foreign currency derivative contracts as Level 2. In certain cases, where there is limited activity or less transparency around inputs to valuation, securities or derivative liabilities such as the Exit Fee, as defined and discussed in Note 4, are classified as Level 3.

The carrying amounts reflected in the balance sheets for cash equivalents, short-term investments, accounts receivable, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values at both March 31, 2021 and December 31, 2020, due to their short-term nature.

Fair Value of Debt

The interest rate of our term loan facility approximates the rate at which we could obtain alternative financing. Therefore, the carrying amount of the term loan facility approximated its fair value at March 31, 2021 and December 31, 2020.

NOTE 4. COLLABORATION AND LICENSING AGREEMENTS

Kyowa Kirin Co., Ltd. ("KKC")

2019 KKC Agreement

In November 2019, we entered into a research collaboration and option agreement with KKC (the "2019 KKC Agreement") for research associated with identifying two preclinical compounds that are ready for designation as development compounds ("DCs"), with one compound inhibiting the first undisclosed target ("Program 1"), and a second inhibiting the second undisclosed target ("Program 2"). Pursuant to the 2019 KKC Agreement, upon completion of the research and designation by the research steering committee of one or more DCs, KKC has the right to execute one or more separate collaborative agreements relating to the development and commercialization of one or both DCs in certain specified territories.

Under the terms of the 2019 KKC Agreement, KKC agreed to pay us a non-refundable, non-creditable upfront fee of $10.0 million, payable as follows: the first installment of $5.0 million within 30 days of November 11, 2019 (the "Effective Date"), and the second installment of $5.0 million on the first anniversary of the Effective Date, unless the 2019 KKC Agreement is earlier terminated by KKC due to material breach by us. The term of the 2019 KKC Agreement commenced on the Effective Date and ends on the earliest of: (i) 2 years following the Effective Date, (ii) the nomination of a program DC for both programs, (iii) the nomination of one program DC and the decision by the parties to cease research for the other program, or (iv) the decision by the parties to cease research for both programs.

During the three months ended March 31, 2021, we recognized $1.5 million as revenue under the 2019 KKC Agreement in the accompanying condensed statement of operations and comprehensive loss. The aggregate amount of the transaction price allocated to our partially unsatisfied performance obligations as of March 31, 2021 was $2.7 million which is presented in the accompanying condensed balance sheet as deferred revenue. As of March 31, 2021, we expect to recognize the remaining transaction price allocated to our partially unsatisfied performance obligations over the remaining research terms, which is currently expected to extend through the end of 2021. There were no significant changes in estimates associated with the 2019 KKC Agreement during the three months ended March 31, 2021.

2017 KKC Agreement

In November 2017, we entered into an exclusive license agreement with KKC (the "2017 KKC Agreement"), for the development, commercialization, and distribution of tenapanor in Japan for cardiorenal indications. We granted KKC an exclusive license to develop and commercialize certain sodium hydrogen exchanger 3 ("NHE3") inhibitors including tenapanor in Japan for the treatment of cardiorenal diseases and conditions, excluding cancer. We retained the rights to tenapanor outside of Japan, and also retained the rights to tenapanor in Japan for indications other than those stated above. Pursuant to the 2017 KKC Agreement, KKC is responsible for all costs and expenses incurred in the development and commercialization of tenapanor for all licensed indications in Japan. We are responsible for supplying the tenapanor drug substance for KKC's use in development and commercialization throughout the term of the 2017 KKC Agreement, provided that KKC may exercise an option to manufacture the tenapanor drug substance under certain conditions.

We assessed these arrangements in accordance with Accounting Standards Update ("ASU") No. 2014-09, *Revenue from Contracts with Customers (Topic 606) and related amendments ("ASC 606")* and concluded that the contract counterparty, KKC, is a customer. Under the terms of the 2017 KKC Agreement, we received $30.0 million in upfront license fees, which was recognized as revenue when the agreement was executed. Based on our assessment, management determined that the license and the manufacturing supply services were its material performance obligations at the inception of the 2017 KKC Agreement, and as such, each of the performance obligations is distinct.

In addition to the up-front license fee received of $30.0 million, we may be entitled to receive up to $55.0 million in total development milestones, of which $10.0 million has been recognized as revenue and $5.0 million has been received as of March 31, 2021, and approximately ¥8.5 billion for commercialization milestones, or approximately $76.5 million at the currency exchange rate on March 31, 2021, as well as reimbursement of costs plus a reasonable overhead for the supply of product and high-teen royalties on net sales throughout the term of the agreement. The variable consideration related to the remaining development milestone payments has not been included in the transaction price as these were fully constrained at March 31, 2021.

During the three months ended March 31, 2021 and 2020, we recognized $5.0 million and zero, respectively, as licensing revenue upon the achievement of development milestones. The $5.0 million development milestone recognized during the three months ended March 31, 2021 related to the initiation by KKC of phase 3 clinical studies in Japan to evaluate tenapanor for

hyperphosphatemia. During the three months ended March 31, 2021, we recognized $0.1 million as product supply revenue related to the manufacturing supply of tenapanor and other materials to KKC pursuant to the 2017 KKC Agreement. Similarly, for the three months ended March 31, 2020, $13.0 thousand was recognized as product supply revenue.

During the three months ended March 31, 2021 we recorded a $2.9 million prepayment that is due to us from KKC for the manufacturing of tenapanor drug substance. The prepayment is reflected within prepaid and other current assets and deferred revenue, non-current on our condensed balance sheet as of March 31, 2021.

Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd. ("Fosun Pharma")

In December 2017, we entered into an exclusive license agreement with Fosun Pharma (the "Fosun Agreement"), for the development, commercialization and distribution of tenapanor in China for both hyperphosphatemia and IBS-C. We assessed these arrangements in accordance with ASC 606 and concluded that the contract counterparty, Fosun Pharma, is a customer. Under the terms of the Fosun Agreement, we received $12.0 million in upfront license fees which was recognized as revenue when the agreement was executed. Based on management's assessment, we determined that the license and the manufacturing supply services represented the material performance obligations at the inception of the agreement, and as such, each of the performance obligations is distinct.

We may be entitled to additional development and commercialization milestones of up to $110.0 million, as well as reimbursement of cost plus a reasonable overhead for the supply of product and tiered royalties on net sales ranging from the mid-teens to 20%. The variable consideration related to the remaining development milestone payments has not been included in the transaction price as these were fully constrained at March 31, 2021.

We have recorded no revenue during the three months ended March 31, 2021 related to the Fosun Agreement.

Knight Therapeutics, Inc. ("Knight")

In March 2018, we entered into an exclusive license agreement with Knight (the "Knight Agreement"), for the development, commercialization and distribution of tenapanor in Canada for hyperphosphatemia and IBS-C. We assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, Knight, is a customer. Based on management's assessment, we determined that the license and the manufacturing supply services represented the material performance obligations at the inception of the agreement, and as such, each of the performance obligations is distinct. Under the terms of the agreement, we received a $2.3 million nonrefundable, one-time upfront payment in March 2018 and are eligible to receive additional development and commercialization milestone payments worth up to $17.6 million. We are also eligible to receive royalties throughout the term of the agreement, and a transfer price for manufacturing services. The variable consideration related to the remaining development milestone payments has not been included in the transaction price as they were fully constrained at March 31, 2021.

AstraZeneca AB ("AstraZeneca")

In June 2015, we entered into a termination agreement with AstraZeneca (the "AstraZeneca Termination Agreement") pursuant to which we have agreed to pay AstraZeneca (i) future royalties at a royalty rate of 10% of net sales of tenapanor or other NHE3 products by us or our licensees, and (ii) 20% of non-royalty revenue received from a new collaboration partner should we elect to license, or otherwise provide rights to develop and commercialize tenapanor or another NHE3 inhibitor, up to a maximum of $75.0 million in aggregate for (i) and (ii). As of March 31, 2021, to date in aggregate, we have recognized $11.6 million of the $75.0 million, which has been recorded as cost of revenue, and have paid AstraZeneca $10.6 million. For the three months ended March 31, 2021 we recognized and recorded as cost of revenue $1.0 million related to the AstraZeneca Termination Agreement. For the three months ended March 31, 2020 we recognized no cost of revenue related to the AstraZeneca Termination Agreement.

Deferred Revenue

The following tables present changes in our current and non-current deferred revenue balances during the reporting period. The current deferred revenue balance is attributable entirely to the 2019 KKC Agreement and the non-current deferred revenue balance is attributable entirely to the 2017 KKC Agreement.

	Deferred revenue - current
Balance at December 31, 2020	$ 4,177
Decreases due to revenue recognized in the period for which cash has been received	(1,454)
Balance at March 31, 2021	$ 2,723

	Deferred revenue non-current
Balance at December 31, 2020	$ -
Increases to amounts invoiced, for which cash has not yet been received	2,9
Balance at March 31, 2021	$ 2,9

NOTE 5. BORROWING

Solar Capital and Western Alliance Bank Loan Agreement

On May 16, 2018, we entered into a loan and security agreement (the “Loan Agreement”), with Solar Capital Ltd. and Western Alliance Bank (collectively the “Lenders”). The Loan Agreement provides for a $50.0 million term loan facility with a maturity date of November 1, 2022 (the “Term Loan”).

On October 9, 2020, we and the Lenders entered into an amendment to the Loan Agreement (“the 2020 Amendment”) to extend the date through which we are permitted to make interest-only payments on the Term Loan by twelve months to December 1, 2021. The 2020 amendment also requires that if either the FDA does not approve our New Drug Application ("NDA") for tenapanor for the control of serum phosphorus in adult patients with chronic kidney disease ("CKD") on dialysis on or before May 31, 2021 or the U.S. Food and Drug Administration ("FDA") issues a CRL with respect to our NDA Number 213931, then we are to begin principal payments on the earlier of June 1, 2021 or the first day of the month immediately following the date that the FDA issues us a CRL. On April 29, 2021, the FDA extended the Prescription Drug User Fee Act ("PDUFA") date for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis by three months to July 29, 2021, making it unlikely that the FDA would approve our NDA for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis on or before May 31, 2021.

In May 2021, we and the Lenders entered into an additional amendment to the Loan Agreement (“the 2021 Amendment”) to extend the date by which FDA approval is required in order to continue interest-only payments through December 1, 2021. The 2021 Amendment requires that if either the FDA does not approve our NDA Number 213931 for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis on or before July 31, 2021 or the FDA issues a complete response letter (“CRL”) for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis, then we are to begin principal payments on the earlier of August 1, 2021 or the first day of the month immediately following the date that the FDA issues us a CRL. If principal repayments are required to begin prior to December 1, 2021 under the 2021 Amendment then the first principal repayment would include all payments that would have been due if principal repayment had begun on June 1, 2021.

We paid a closing fee of 1% of the Term Loan, or $0.5 million, upon the closing of the Term Loan, and $0.1 million upon closing of the 2020 Amendment. Under the Term Loan, we are also obligated to pay a final fee equal to 4.95% of the Term Loan upon the earliest to occur of the maturity date, the acceleration of the Term Loan, the prepayment or repayment of the Term Loan or the termination of the Loan Agreement. We may voluntarily prepay the outstanding Term Loan, subject to a prepayment premium of (i) 3% of the principal amount of the Term Loan if prepaid prior to or on the first anniversary of the Closing Date, (ii) 2% of the principal amount of the Term Loan if prepaid after the first anniversary of the Closing Date through and including the second anniversary of the Closing Date, or (iii) 1% of the principal amount of the Term Loan if prepaid after the second anniversary of the Closing Date and prior to the maturity date. The Term Loan is secured by substantially all our assets, except for our intellectual property and certain other customary exclusions. Additionally, in connection with the Term Loan, we entered into the Exit Fee Agreement, as discussed in Note 6.

The Loan Agreement also contains customary events of default that entitle the Lender to cause us indebtedness under the Loan Agreement to become immediately due and payable, and to exercise remedies against us and the collateral securing the Term Loan, including our cash. Upon the occurrence and for the duration of an event of default, an additional default interest

rate equal to 4% per annum will apply to all amounts owed under the Loan Agreement. As of March 31, 2021, to our knowledge, there were no facts or circumstances in existence that would give rise to an event of default.

As of March 31, 2021, our future payment obligations related to the Term Loan, excluding interest payments and the Exit Fee, are as follows (in thousands):

Total repayment obligations	$	52,475
Less: Unamortized discount and debt issuance costs		(449)
Less: Unaccreted value of final fee		(1,011)
Loan payable		51,015
Less: Loan payable, current portion		(16,667)
Loan payable, net of current portion	$	34,348

NOTE 6. DERIVATIVE LIABILITY

Exit Fee

In May 2018, in connection with entering into the Loan Agreement, as defined and discussed in Note 5, we entered into an agreement pursuant to which we agreed to pay $1.5 million in cash (the "Exit Fee") upon any change of control transaction in respect of the Company or if we obtain both (i) FDA approval of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis and (ii) FDA approval of tenapanor for the treatment of patients with irritable bowel syndrome with constipation ("IBS-C"), which was obtained on September 12, 2019 when the FDA approved IBSRELA® (tenapanor), a 50 milligram, twice daily oral pill for the treatment of IBS-C in adults (the "Exit Fee Agreement"). Notwithstanding the prepayment or termination of the Term Loan, as defined and discussed in Note 5, our obligation to pay the Exit Fee will expire on May 16, 2028. We concluded that the Exit Fee is a freestanding derivative which should be accounted for at fair value on a recurring basis. The estimated fair value of the Exit Fee is recorded as a derivative liability and included in accrued expenses and other current liabilities on the accompanying condensed balance sheets.

The fair value of the derivative liability was determined using a discounted cash flow analysis and is classified as a Level 3 measurement within the fair value hierarchy since our valuation utilized significant unobservable inputs. Specifically, the key assumptions included in the calculation of the estimated fair value of the derivative liability include: (i) our estimates of both the probability and timing of a potential $1.5 million payment to Solar Capital Ltd. and Western Alliance Bank as a result of the FDA approvals and (ii) a discount rate which was derived from our estimated cost of debt, adjusted with current LIBOR (or a comparable successor rate if LIBOR no longer exists). Generally, increases or decreases in the probability of occurrence would result in a directionally similar impact in the fair value measurement of the derivative liability and it is estimated that a 10% increase (decrease), not to exceed 100%, in the probability of occurrence would result in a fair value fluctuation of no more than $0.1 million.

Changes in the fair value of recurring measurements included in Level 3 of the fair value hierarchy are presented as other income (expense), net in our statements of operations and were as follows for the three months ended March 31, 2021 and 2020 (in thousands):

	Three Months Ended March 31,			
		2021		2020
Fair value of Exit Fee derivative liability at January 1	$	1,376	$	969
Change in estimated fair value of derivative liability		36		82
Fair value of Exit Fee derivative liability at March 31	$	1,412	$	1,051

NOTE 7. LEASES

All of our leases are operating leases and each contain customary rent escalation clauses. Certain of the leases have both lease and non-lease components. We have elected to account for each separate lease component and the non-lease components associated with that lease component as a single lease component for all classes of underlying assets.

The following table provides additional details of our facility leases presented in the condensed balance sheet as of March 31, 2021 (dollars in thousands):

Facilities		
Right of use assets	$	1,667
Current portion of lease liabilities		1,412
Operating lease liability, net of current portion		397
Total	$	1,809
Weighted-average remaining life (years)		1.60
Weighted-average discount rate		11.23 %

Lease costs, which are included in operating expenses in our statements of operations, were as follows (in thousands):

	Three Months Ended March 31,	
	2021	2020
Operating lease expense	$ 673	$ 648
Cash paid for operating leases	$ 1,565	$ 760

The following table summarizes our undiscounted cash payment obligations for our operating lease liabilities as of March 31, 2021:

Remainder of 2021	$ 1,463
Thereafter	469
Total undiscounted operating lease payments	1,932
Imputed interest expenses	(123)
Total operating lease liabilities	1,809
Less: Current portion of operating lease liability	(1,412)
Operating lease liability, net of current portion	$ 397

NOTE 8. STOCKHOLDERS' EQUITY

At the Market Offerings Agreement

In July 2020, we filed a Form S-3 registration statement, which became effective in August 2020, containing (i) a base prospectus for the offering, issuance and sale by us of up to a maximum aggregate offering price of $250.0 million of our common stock, preferred stock, debt securities, warrants and/or units, from time to time in one or more offerings; and (ii) a prospectus supplement for the offering, issuance and sale by us of up to a maximum aggregate offering price of $100.0 million of our common stock that may be issued and sold, from time to time, under a sales agreement with Jefferies LLC, deemed to be "at the market offerings." During the three months ended March 31, 2021, we sold 4.9 million shares of our common stock for aggregate gross proceeds of $35.0 million at a weighted average price of $7.09 per share under the Open Market Sales Agreement. In aggregate during the life of the Open Market Sales Agreement, and as of March 31, 2021, we have sold 8.2 million shares of our common stock for gross proceeds of $56.7 million at a weighted average sales price of approximately $6.91 per share. Pursuant to the Open Market Sales Agreement, Jefferies, as sales agent, receives a commission of up to 3.0% of the gross sales price for shares of common stock sold under the Open Market Sales Agreement.

NOTE 9. EQUITY INCENTIVE PLANS

Stock Option Plan

During the three months ended March 31, 2021, options were granted to employees and members of the board of directors to purchase 2.8 million shares of our common stock. The weighted-average grant-date estimated fair value of options granted during the three months ended March 31, 2021 was $6.51.

During the three months ended March 31, 2021, options were exercised to purchase 10.5 thousand shares of our common stock, resulting in net proceeds of approximately $0.5 million. During the three months ended March 31, 2020, options were exercised to purchase 0.1 million shares of or common stock, resulting in net proceeds of approximately $0.6 million.

Restricted Stock Units

During the three months ended March 31, 2021, we granted 0.9 million restricted stock units (“RSUs”) to our employees that will vest upon employees’ continued service relationship with us. During the three months ended March 31, 2020, we granted 0.9 million restricted stock units to our employees.

During both the three months ended March 31, 2021 and March 31, 2020, we granted no performance-based restricted stock units ("PRSUs") to our employees.

Employee Stock Purchase Plan

In February 2021, we sold 0.2 million shares of our common stock under our employee stock purchase program (the "ESPP"). The shares were purchased by employees at a purchase price of $5.84 per share resulting in proceeds to us of approximately $1.4 million.

Issuance of Common Stock for Services

Under Our Amended and Restated Non-Employee Director Compensation Program, members of our board of directors may elect to receive shares of our stock in lieu of their cash fees. For the three months ended March 31, 2021 and 2020, we issued no shares of our common stock to members of the board of directors in accordance with the program.

Stock-Based Compensation

Stock-based compensation expense recognized for stock options, RSUs, PRSUs and the ESPP are recorded as operating expenses in our condensed statements of operations and comprehensive loss, as follows:

	Three Months Ended March 31,	
	2021	2020
Research and development	$ 1,092	$ 1,058
General and administrative	1,995	1,890
Total	$ 3,087	$ 2,948

As of March 31, 2021, our total unrecognized stock-based compensation expense, net of estimated forfeitures, and average remaining vesting period, included the following:

	Unrecognized Compensation Expense	Average Remaining Vesting Period (Years)
Stock options	$ 25,723	3.1
RSUs	$ 6,246	3.7
ESPP	$ 399	0.4

NOTE 10. NET LOSS PER SHARE

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period, less shares subject to repurchase, and excludes any dilutive effects of stock-based awards and warrants. Diluted net loss per common share is computed giving effect to all potential dilutive common shares, including common stock issuable upon exercise of stock options, and unvested restricted common stock and stock units. As we had net losses for the

three months ended March 31, 2021 and 2020, all potential common shares were determined to be anti-dilutive. The following table sets forth the computation of net loss per common share:

	Three Months Ended March 31,	
	2021	2020
Numerator:		
Net loss	$ (33,155)	$ (22,373)
Denominator:		
Weighted average common shares outstanding - basic and diluted	97,179,241	88,880,658
Net loss per share - basic and diluted	$ (0.34)	$ (0.25)

For the three months ended March 31, 2021, the total number of securities that could potentially dilute basic net loss per share in the future that were not included in the computation of diluted net loss per share because the effect would have been antidilutive was 13.0 million.

For the three months ended March 31, 2020, the total number of securities that could potentially dilute basic net loss per share in the future that were not included in the computation of diluted net loss per share because the effect would have been antidilutive was 11.9 million.

NOTE 11. CONTINGENCIES

From time to time we may be involved in claims arising in connection with our business. Based on information currently available, management believes that the amount, or range, of reasonably possible losses in connection with any pending actions against us would not be material to our financial condition or cash flows, and no contingent liabilities were accrued as of March 31, 2021 or 2020.

NOTE 12. SUBSEQUENT EVENTS

On April 29, 2021, the FDA extended the PDUFA date for our NDA for tenapanor for control of serum phosphorus in adult patients with CKD on dialysis by three months to July 29, 2021.

In May 2021, we entered into an amendment to our loan and security agreement (the “Loan Agreement”), with Solar Capital Ltd. and Western Alliance Bank (collectively the “Lenders”) to extend the date by which FDA approval is required in order to continue interest-only payments through December 1, 2021. Please see Note 5. Borrowing for additional information.

ITEM 2. MANAGEMENT’S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the condensed financial statements and notes thereto included elsewhere in this report and with the audited financial statements and related notes thereto included as part of our Annual Report on Form 10-K for the year ended December 31, 2020. This discussion and analysis and other parts of this report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section of this report entitled “Risk Factors.” These forward-looking statements speak only as of the date hereof. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason. Unless the context requires otherwise, the terms “Ardelyx”, “Company”, “we”, “us”, and “our” refer to Ardelyx, Inc.

OVERVIEW

We are a specialized biopharmaceutical company focused on discovering, developing and commercializing innovative first-in-class medicines to enhance the lives of patients with kidney and cardiorenal diseases. This includes patients with chronic kidney disease ("CKD") on dialysis suffering from elevated serum phosphorus, or hyperphosphatemia; and CKD patients and/or heart failure patients with elevated serum potassium, or hyperkalemia. Tenapanor has a unique mechanism of action and acts locally in the gut to inhibit the sodium hydrogen exchanger 3, or NHE3. This results in the tightening of the epithelial cell junctions, thereby significantly reducing paracellular uptake of phosphate, the primary pathway of phosphate absorption.

OUR PRODUCT PIPELINE

Tenapanor: A New Approach for The Control of Serum Phosphorus in CKD Patients on Dialysis

Our portfolio is led by the development of tenapanor, a first-in-class medicine for the control of serum phosphorus in adult patients with CKD on dialysis. Tenapanor for the control of serum phosphorus has a unique mechanism of action and acts locally in the gut to inhibit the sodium hydrogen exchanger 3 ("NHE3"). This results in the tightening of the epithelial cell junctions, thereby significantly reducing paracellular uptake of phosphate, the primary pathway of phosphate absorption. On April 29, 2021, the U.S. Food and Drug Administration ("FDA") determined that a submission we made in response to an information request from the FDA constituted a major amendment to our New Drug Application ("NDA") for tenapanor for the control of serum phosphorus, resulting in a three-month extension of the PDUFA date to July 29, 2021. The FDA's information request included a request for additional analyses of our clinical data.

We have exclusive rights to tenapanor in the U.S. and we have established agreements with Kyowa Kirin Co., Ltd. ("KKC") in Japan, Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd. ("Fosun Pharma") in China and Knight Therapeutics, Inc. ("Knight") in Canada for the development and commercialization of tenapanor for certain indications in their respective territories.

In December 2019, we reported statistically significant topline efficacy results from our second monotherapy Phase 3 clinical trial, the PHREEDOM trial, which evaluated tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis. The PHREEDOM trial followed a successful monotherapy Phase 3 clinical trial completed in 2017, the BLOCK trial, which achieved statistical significance for the primary endpoint. The only adverse event reported in these Phase 3 trials in less than 5% of patients was diarrhea, with an incidence rate of 52% in the PHREEDOM trial and 39% in the BLOCK trial, with most incidences in each trial being mild to moderate in nature. PHREEDOM is a one-year study with a 26-week open-label treatment period and a 12-week double-blind, placebo-controlled randomized withdrawal period followed by a 14-week open-label safety extension period. An active safety control group, for safety analysis only, received sevelamer, open-label, for the entire 52-week study period. Patients completing the PHREEDOM trial from both the tenapanor arm and the sevelamer active safety control arm had the option to participate in NORMALIZE, an ongoing open-label 18-month extension study.

In June 2020, we announced positive results from a planned interim data analysis from our ongoing NORMALIZE extension study evaluating tenapanor, as monotherapy or in combination with sevelamer, to achieve serum phosphorus levels in the normal range (2.5 – 4.5 mg/dL) in patients with CKD on dialysis. The NORMALIZE extension study allowed patients from our PHREEDOM study to continue therapy with tenapanor and enabled those patients in the PHREEDOM safety control arm receiving sevelamer carbonate to transition to tenapanor. The data from the planned interim analysis demonstrated that the use of tenapanor as monotherapy or in combination with sevelamer carbonate produces a significant phosphorus-lowering effect with a mean serum phosphorous reduction of 2.33 mg/dL, from a mean baseline phosphorus of 7.27 mg/dL at the beginning of the PHREEDOM trial to a mean of 4.94 mg/dL at the time of this analysis. Of the 171 patients in this interim analysis who completed up to 9 months of treatment in this extension study, up to 47.4% achieved a normal serum phosphorus level, and of those, the majority were on tenapanor alone or tenapanor with low dose sevelamer of three or fewer sevelamer tablets per day. These data represent a 58% improvement in the rate of patients who achieve a normal serum phosphorus level, as compared to current treatment practice data as reported in the April 2020 Dialysis Outcomes Practice Patterns Study ("DOPPS") Practice Monitor. The DOPPS data demonstrate that, with currently available treatments, only 30% of patients have serum phosphorous levels less than 4.6 mg/dL. The only adverse event reported in greater than 5% of patients in NORMALIZE was diarrhea, with an incidence rate of 23.3%.

In September 2019, we reported positive results from the AMPLIFY trial, a Phase 3 study evaluating tenapanor in patients with CKD on dialysis who had uncontrolled hyperphosphatemia despite phosphate binder treatment. In this trial, approximately twice the number of patients achieved the serum phosphorus treatment goal of less than 5.5 mg/dL with tenapanor and phosphate binders versus phosphate binders alone. The only adverse event with a placebo-adjusted rate greater than 3% was diarrhea, with an incidence rate of 43%, with most being mild to moderate in nature.

In June 2020, our partner KKC, a Japan-based global specialty pharmaceutical company exclusively developing tenapanor in Japan, presented results from a Phase 2 trial of tenapanor at the European Renal Association-European Dialysis and Transplant Association annual meeting ("ERA-EDTA 2020"). The trial was designed to evaluate if, with tenapanor, patients with hyperphosphatemia undergoing hemodialysis could achieve at least a 30% decrease in mean pill burden while maintaining their serum phosphorus level. The study results were statistically significant, with 71.6% ($p<0.001$) of patients achieving at least a 30% reduction in mean pill burden. The overall mean reduction in phosphate binder usage was 80% (reduction from 14.7 to 3.0 pills per day), while maintaining serum phosphorus control. The mean phosphorus level of patients entering the study on treatment with binders was 5.2 mg/dL at baseline and 4.7 mg/dL at the end of the 26-week study.

Tenapanor is the first therapy for phosphate management that blocks phosphorus absorption at the primary pathway of uptake. It is not a phosphate binder. Tenapanor is a novel, potent, small molecule, that has been shown in phase 3 studies to treat hyperphosphatemia as monotherapy and as a dual mechanism approach.

IBSRELA® (tenapanor) for Irritable Bowel Syndrome with Constipation (IBS-C)

In addition to the development of tenapanor for hyperphosphatemia, we have developed tenapanor for the treatment of patients with irritable bowel syndrome with constipation ("IBS-C"). In September 2019, we received FDA approval of IBSRELA® (tenapanor) for the treatment of IBS-C in adults. IBS-C is a burdensome gastrointestinal ("GI") disorder. It is characterized by significant abdominal pain, constipation, straining during bowel movements, bloating and/or gas.

RDX013 Program: Small Molecule for Treating Hyperkalemia

We are also advancing a small molecule potassium secretagogue program, RDX013, for the potential treatment of hyperkalemia. Hyperkalemia is a common problem in patients with heart and kidney disease, particularly in patients taking common blood pressure medications known as renin-angiotensin-aldosterone system ("RAAS") inhibitors. Similar to what we have done with tenapanor in developing a non-binder approach for the treatment of elevated serum phosphate levels, RDX013 is designed to target the underlying biological mechanisms of potassium secretion to lower elevated potassium. While currently available therapies are all ion exchange agents, RDX013 is a first in class approach that exerts its effects by amplifying the underlying pathways of potassium secretion in the colon.

Since commencing operations in October 2007, substantially all our efforts have been dedicated to our research and development ("R&D") activities, including developing our clinical product candidate tenapanor and developing our proprietary drug discovery and design platform. We have not generated any revenues from product sales. As of March 31, 2021, we had an accumulated deficit of $587.9 million.

We expect to continue to incur substantial operating losses for the foreseeable future as a result of costs associated with the following activities: our continued development of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis; our preparations for, and if approved, the commercialization of tenapanor in the United States for the control of serum phosphorus in adult patients with CKD on dialysis, or for any related indication, including significantly increased personnel costs associated with our commercial team; the performance of certain activities required as a result of our NDA approval of tenapanor for IBS-C; the continued development of RDX013 and the advancement of our research programs into the preclinical stage. To date, we have funded our operations from the sale and issuance of common stock and convertible preferred stock, funds from our collaboration partnerships, which includes license fees, milestones and product supply revenue, as well as funds from our Loan Agreement with Solar Capital Ltd. and Western Alliance Bank.

RDX020 Program: Small molecule for Treating Metabolic Acidosis

We have an ongoing discovery program targeting the inhibition of bicarbonate exchange inhibitor for the treatment of metabolic acidosis, a highly prevalent comorbidity in CKD patients that is strongly correlated with disease progression and adverse outcomes. We have identified lead compounds that are potent, selective and proprietary inhibitors of bicarbonate secretion.

Impact of COVID-19

The global COVID-19 pandemic has impacted the operational decisions of companies worldwide. It also has created and may continue to create significant uncertainty in the global economy. We have undertaken measures to protect our employees, partners, collaborators, and vendors, some of which impact our normal operations. To date, we have been able to continue our operations with our workforce, most of whom are working remotely, and our pre-existing infrastructure that supports secure access to our internal systems. If, however, the COVID-19 pandemic has a substantial impact on the productivity of our employees, our ability to successfully prepare for the commercial launch of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis, including our ability to hire and successfully integrate into the company the new personnel required to prepare for such launch, or our ability to progress our research and development efforts, the results of our operations and overall financial performance may be adversely impacted. The extent of the impact from the COVID-19 pandemic on our business will depend largely on future developments that are highly uncertain and cannot be predicted. For a discussion of risks of COVID-19 relating to our business, see "Part II: Other Information-Item 1A.- Risk Factors- Risks Related to Our Business- *The ongoing COVID-19 pandemic, or any other outbreak of epidemic diseases, or the perception of their effects, could have a material adverse effect on our business, financial condition, results of operations or cash flows*." As of the date of issuance of this financial report, we are not aware of any specific event or circumstance that would require updates to our estimates and

judgments or revisions to the carrying value of our assets or liabilities. These estimates may change as new events occur and additional information is obtained.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of financial condition and results of operations is based on our condensed financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States.

Critical accounting policies are those that require significant judgment and/or estimates by management at the time that financial statements are prepared such that materially different results might have been reported if other assumptions had been made. These estimates form the basis for making judgments about the carrying values of assets and liabilities. We base our estimates and judgments on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results could differ materially from these estimates.

The critical accounting policies that we believe impact significant judgments and estimates used in the preparation of our financial statements presented in this report are described in Part II, Item 7, *Management's Discussion and Analysis of Financial Condition and Results of Operations*, in our Annual Report on Form 10-K filed with the SEC on March 8, 2021. There have been no significant changes to our critical accounting policies as disclosed in our most recently filed Annual Report on Form 10-K during the three months ended March 31, 2021.

Recent Accounting Pronouncements

A summary of recent accounting pronouncements that we have adopted or may expect to adopt is included in Note 1 – Organization and Basis of Presentation to our condensed financial statements (see Part I, Item 1 *Notes to Condensed Financial Statements*, of this Quarterly Report on Form 10-Q).

Financial Operations Overview

Revenue

Our revenue to date has been generated primarily through license, research and development collaborative agreements with various collaboration partners. We have not generated any revenue from commercial product sales. In the future, we may generate revenue from a combination of our own product sales, if regulatory approval is received, and payments in connection with our current or future collaborative partnerships, including license fees, other upfront payments, milestone payments, royalties and payments for drug product and/or drug substance. We expect that any revenue we generate will fluctuate in future periods as a result of, among other factors: whether we receive regulatory approval for tenapanor for the control of serum phosphorus in CDK patients on dialysis, and if such approval is received, the timing of such approval and the extent to which we are successful in our efforts to commercialize tenapanor for such indication; the timing and progress of goods and services provided pursuant to our current or future collaborative partnerships; our or our collaborators' achievement of preclinical, clinical, regulatory or commercialization milestones, to the extent achieved; the timing and amount of any payments to us relating to the aforementioned milestones; and the extent to which any of our product candidates are approved and successfully commercialized by a collaboration partner. If our current collaboration partners or any future collaboration partners fail to obtain regulatory approval for tenapanor, our ability to generate future revenue from our product sales or from our collaborative arrangements, and our results of operations and financial position, would be materially and adversely affected. Our past revenue performance is not necessarily indicative of results to be expected in future periods.

Cost of Revenue

Cost of revenue currently represents payments due to AstraZeneca, which under the terms of a termination agreement entered into in 2015 is entitled to (i) future royalties at a rate of 10% of net sales of tenapanor or other NHE3 products by us or our licensees, and (ii) 20% of non-royalty revenue received from our collaboration partners should we elect to which we provide rights to develop and commercialize tenapanor or certain other NHE3 inhibitors. We have agreed to pay AstraZeneca up to a maximum of $75.0 million in the aggregate for (i) and (ii). We recognize these expenses as cost of revenue when we recognize the corresponding revenue that gives rise to payments due to AstraZeneca. To date, we have recognized an aggregate of $11.6 million as cost of revenue under the AZ Termination Agreement since 2017.

Research and Development

We recognize all research and development expenses as they are incurred to support the discovery, research, development and manufacturing of our product candidates. Research and development expenses include, but are not limited to, the following:

- external research and development expenses incurred under agreements with consultants, third-party contract research organizations ("CROs") and investigative sites where a substantial portion of our clinical studies are conducted, and with contract manufacturing organizations where our clinical supplies are produced;
- expenses associated with supplies and materials consumed in connection with our research operations;
- expenses associated with producing tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis prior to FDA approval;
- other costs associated with research, clinical development and regulatory activities; and
- employee-related expenses, which include salaries, bonuses, benefits, travel and stock-based compensation;
- facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation and amortization expense, information technology expense and other supplies.

We expect to continue to make substantial investments in research and development activities as we further progress the development of tenapanor, particularly if the FDA should require additional clinical trials in connection with our NDA for the control of serum phosphorus in adult patients with CKD on dialysis, RDX013 and our other product candidates, as we advance our research programs into the preclinical stage and as we continue our early stage research. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time-consuming. On April 29, 2021, the FDA determined that a submission we made in response to an information request from the FDA constituted a major amendment to our NDA for tenapanor for the control of serum phosphorus, resulting in a three-month extension of the PDUFA date to July 29, 2021. The FDA's information request included a request for additional analyses of our clinical data. The FDA may act on our application either by issuing an approval letter or by issuing a Complete Response Letter ("CRL"). Should we wish to pursue our application after receiving a CRL, we can, if possible, resubmit the application with information that addresses the questions or issues identified by the FDA in order to support approval. Resubmissions are subject to review period targets, which vary depending on the underlying submission type and the content of the resubmission. We may not succeed in achieving marketing approval for our product candidates, including tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis. The probability of success of each of the product candidates may be affected by numerous factors, including preclinical data, clinical data, the regulatory process, market acceptance, sufficient third-party coverage or reimbursement, our ability to access capital on acceptable terms, competition, manufacturing capability and commercial viability.

We anticipate that we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each product candidate, ongoing assessment as to each product candidate's commercial potential, and our ability to access capital on acceptable terms. We will need to raise additional capital to complete the development and commercialization of tenapanor. If we are unable to access capital on a timely basis and on terms that are acceptable to us, we may be forced to restructure certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the development or commercialization of tenapanor, the development of RDX013 or certain of our product candidates through the use of alternative structures.

General and Administrative

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, for certain of our executives, our board members, and our finance, legal, business development, market development, commercial and support staff. Other general and administrative expenses include facility related costs and professional fees for legal, accounting and audit, investor relations, other consulting services and allocated facility-related costs not otherwise included in research and development expenses.

We anticipate that our general and administrative expenses will increase in the future primarily because of increased pre-commercial and commercial activities, personnel costs and professional fees for services to support the potential launch and commercialization of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis.

Interest Expense

Interest expense represents the interest paid on our loan payable.

Other Income, net

Other income, net consists of interest income earned on our cash and cash equivalents and available-for-sale investments, the periodic revaluation of the exit fee related to our loan and currency exchange gains and losses.

RESULTS OF OPERATIONS

The results of operations are not necessarily indicative of the results to be expected for the year ending December 31, 2021, for any other interim period, or for any other future year.

Comparison of the three months ended March 31, 2021 and 2020

Revenue

Below is a summary of our total revenue (dollar amounts in thousands):

	Three Months Ended March 31,		Change	
	2021	2020	$	%
Collaborative development revenue	$ 1,454	$ 1,175	$ 279	23.7 %
Product supply revenue	126	38	88	231.6 %
Licensing revenue	5,002	—	5,002	(a)
Total revenues	$ 6,582	$ 1,213	$ 5,369	442.6 %

(a) Percent change is not meaningful.

The increase to total revenues during the three months ended March 31, 2021 as compared to the same period in 2020 is primarily attributable to a $5.0 million development milestone which we earned upon the initiation by KKC of phase 3 clinical studies in Japan to evaluate tenapanor for hyperphosphatemia. There was no comparable revenue during the three months ended March 31, 2020.

Operating Expenses

Below is a summary of our operating expenses (dollars in thousands):

	Three Months Ended March 31,		Change	
	2021	2020	$	%
Cost of revenue	$ 1,000	$ —	$ 1,000	(a)
Research and development	20,456	15,844	4,612	29.1 %
General and administrative	17,131	7,138	9,993	140.0 %
Total operating expenses	$ 38,587	$ 22,982	$ 15,605	67.9 %

(a) Percent change is not meaningful.

Cost of revenue

The increase in cost of revenue for the three months ended March 31, 2021 was for payment due to AstraZeneca under the AZ Termination Agreement related to the development milestone we earned upon the initiation by KKC of phase 3 clinical studies in Japan to evaluate tenapanor for hyperphosphatemia.

Research and Development

Below is a summary of our research and development expenses (dollars in thousands):

	Three Months Ended March 31,		Change	
	2021	2020	$	%
External R&D expenses	$ 11,508	$ 9,197	$ 2,311	25.1 %
Employee-related expenses	7,220	4,994	2,226	44.6 %
Facilities, equipment and depreciation expenses	1,284	1,593	(309)	(19.4)%
Other	444	60	384	640.0 %
Total research and development expenses	$ 20,456	$ 15,844	$ 4,612	29.1 %

The increase in our external R&D expenses for the three months ended March 31, 2021 is primarily the result of clinical study costs from the advancement of our OPTIMIZE study which were partially offset by lower costs for the PHREEDOM clinical study. The increase in our employee-related expenses for the three months ended March 31, 2021 is related to recruiting, compensation and benefits expenses for our research and development workforce.

General and Administrative

The increase in general and administrative expenses for the three months ended March 31, 2021 was primarily due to an increase in costs associated with building and staffing our commercial infrastructure and teams as we prepare for the U.S. launch of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis. The increase consisted of headcount and related personnel costs and an increase in external spending for disease awareness initiatives, commercial infrastructure and strategy, partially offset by a decrease in stock-based compensation costs related to performance-based restricted stock units.

Other Income (Expense), net

Below is a summary of our other income (expense), net (dollars in thousands):

	Three Months Ended March 31,		Change	
	2021	2020	$	%
Interest expense	$ (1,100)	$ (1,357)	$ 257	(18.9)
Other income (expense), net	(49)	753	(802)	(106.5)
Total other income (expense), net	$ (1,149)	$ (604)	$ (545)	90.2

Interest Expense

The decrease in interest expense for the three months ended March 31, 2021 was primarily due to lower interest rates on our variable-rate term loan.

Other Income, net

The decrease in other income (expense), net for the three months ended March 31, 2021 was primarily due to a decrease in investment income and an increase to the exit fee accretion related to our term loan agreement.

Liquidity and Capital Resources

Below is a summary of our cash, cash equivalents and marketable securities (in thousands):

	March 31, 2021	December 31, 2020
Cash and cash equivalents	$ 84,070	$ 91,032
Marketable securities - current	94,142	95,452
Marketable securities - non-current	—	2,114
Total liquid funds	$ 178,256	$ 188,642

As of March 31, 2021, we had cash, cash equivalents and marketable securities totaling $178.2 million compared to $188.6 million as of December 31, 2020.

In July 2020, we filed a Form S-3 registration statement, which became effective in August 2020, containing (i) a base prospectus for the offering, issuance and sale by us of up to a maximum aggregate offering price of $250.0 million of our common stock, preferred stock, debt securities, warrants and/or units, from time to time in one or more offerings; and (ii) a prospectus supplement for the offering, issuance and sale by us of up to a maximum aggregate offering price of $100.0 million of our common stock that may be issued and sold, from time to time, under a sales agreement with Jefferies LLC, deemed to be “at the market offerings.” During the three months ended March 31, 2021, we sold 4.9 million shares of our common stock for aggregate gross proceeds of $35.0 million at a weighted average price of $7.09 per share under the Open Market Sales Agreement. In aggregate during the life of the Open Market Sales Agreement, and as of March 31, 2021, we have sold 8.2 million shares of our common stock for gross proceeds of $56.7 million at a weighted average sales price of approximately $6.91 per share. Pursuant to the Open Market Sales Agreement, Jefferies, as sales agent, receives a commission of up to 3.0% of the gross sales price for shares of common stock sold under the Open Market Sales Agreement.

Our primary sources of cash have been from the sale and issuance of common stock (in both public offerings and private placements) and private placements of convertible preferred stock, funds from our collaboration partnerships and funds from our loan agreement. Our primary uses of cash are to fund operating expenses, primarily research and development expenditures and pre-commercial expenses. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Funding Requirements

We believe that our existing capital resources as of March 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months following our financial statement issuance date. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. In particular, our operating plan can change, and we may require significant additional capital to fund our operations, including to support the development, commercialization and manufacturing efforts for tenapanor. We may seek to obtain such additional capital through debt financings, credit facilities, additional equity offerings and/or strategic collaborations. We currently have no unutilized credit facility or committed sources of capital, and there can be no assurances that such sources of capital will be available to us when needed or on acceptable terms. There are numerous risks and uncertainties associated with research, development and commercialization initiatives, and actual results could vary materially as a result of a number of factors, many of which are outside of our control. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the FDA’s actions and decisions with respect to the NDA submitted to the FDA on June 30, 2020 to request marketing authorization for tenapanor for the control of serum phosphorus in adult CKD patients on dialysis, including the FDA’s actions after the three-month extension of the PDUFA date to July 29, 2021;
- our ability to successfully commercialize tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication, if approved, either alone or with one or more collaboration partners;
- the sales price and the availability of adequate third-party reimbursement for tenapanor, if approved;
- the manufacturing costs of our product candidates, and the availability of one or more suppliers for our product candidates at reasonable costs, both for clinical and commercial supply;

- the selling and marketing costs associated with tenapanor, including the cost and timing of maintaining our sales and marketing capabilities;
- our ability to maintain our existing collaboration partnerships and to establish additional collaboration partnerships, in-license/out-license, joint ventures or other similar arrangements and the financial terms of such agreements;
- the timing, receipt, and amount of sales of, or royalties on, tenapanor, if any;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the number and scope of preclinical and discovery programs that we decide to pursue or initiate, and any clinical trials we decide to pursue for other product candidates, including RDX013;
- the time and cost necessary to respond to technological and market developments;
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of tenapanor or any of our product candidates; and
- the payment of interest and principal related to our loan and security agreement entered into with Solar Capital and Western Alliance Bank in May 2018, as amended in October 2020.

Please see the risk factors set forth in Part II, Item 1A, Risk Factors, in this Quarterly Report on Form 10-Q for additional risks associated with our capital requirements.

CASH FLOW ACTIVITIES

The following table summarizes our cash flows (in thousands):

	Three Months Ended March 31,	
	2021	**2020**
Cash used in operating activities	$ (44,217)	$ (24,946)
Cash (used in) provided by investing activities	2,485	(50,883)
Cash provided by financing activities	34,770	591
Net decrease in cash and cash equivalents	$ (6,962)	$ (75,238)

Cash Flows from Operating Activities

Net cash used in operating activities during the three months ended March 31, 2021 increased by $19.3 million as a result of our increased net loss for the period. The increased net loss was primarily driven by costs associated with building and staffing our commercial infrastructure and teams as we prepare for the U.S. launch of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis. An increase of $12.7 million of cash used in prepaid expenses and other assets which was primarily for prepayments for raw materials and production of tenapanor also contributed to the increase in net cash used during the three months ended March 31, 2021.

Cash Flows from Investing Activities

Net cash provided by investing activities increased by $53.4 million as a our investment maturities increased to fully offset the cost to purchase investments. During the three months ended March 31, 2020, investment purchases exceeded maturities by approximately $50.9 million.

Cash Flows from Financing Activities

Net cash provided by financing activities increased by $34.2 million due to net proceeds from issuance of our common stock pursuant to the Open Market Sales Agreement, or at-the-market offering.

Off-Balance Sheet Arrangements

As of March 31, 2021 and 2020, respectively, we did not have any off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K as promulgated by the SEC.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk. We are subject to market risks, including interest rate fluctuation exposure through our investments, in the ordinary course of our business. However, the goals of our investment policy are the preservation of capital, fulfillment of liquidity needs and fiduciary control of cash. To achieve our goal of maximizing income without assuming significant market risk, we maintain our excess cash and cash equivalents in money market funds and short-term debt securities. Because of the short-term maturities of our cash equivalents, we do not believe that a decrease in interest rates would have any material negative impact on the fair value of our cash equivalents.

As of March 31, 2021, we had cash, cash equivalents and marketable securities of $178.2 million, which consist of bank deposits and money market funds, as well as high quality fixed income instruments including corporate bonds, commercial paper, and asset-backed securities collateralized by non-mortgage consumer receivables. The credit rating of our short-term investments must be rated A-1/P-1, or better by Standard and Poor's and Moody's Investors Service. Asset-backed securities must be rated AAA/Aaa. Money Market funds must be rated AAAm/Aaa. Such interest-earning instruments carry a degree of interest rate risk. However, because our investments are high quality and short-term in duration, we believe that our exposure to interest rate risk is not significant and that a 10% movement in market interest rates would not have a significant impact on the total value of our portfolio, as noted above. We do not enter into investments for trading or speculative purposes.

We are subject to interest rate fluctuation exposure through our borrowings under the Loan Agreement and our investment in money market accounts which bear a variable interest rate. Borrowings under the Loan Agreement bear interest at a rate equal to one-month London Interbank Offered Rate ("LIBOR"), plus 7.45% per annum. A hypothetical increase in one-month LIBOR of 100 basis points above the current one-month LIBOR rates would have increased our interest expense by approximately $0.1 million for the three months ended March 31, 2021. As of March 31, 2021, we had an aggregate principal amount of $50.0 million outstanding pursuant to our Loan Agreement.

Foreign Currency Risk. The majority of our transactions are denominated in U.S. dollars. However, we do have certain transactions that are denominated in currencies other than the U.S. dollar, primarily Swiss francs and the euro, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against other currencies affects the reported amounts of expenses, assets and liabilities associated with a limited number of manufacturing activities.

We do not use derivative financial instruments for speculative trading purposes, nor do we hedge foreign currency exchange rate exposure in a manner that entirely offsets the earnings effects of changes in foreign currency exchange rates. The counterparties to our forward foreign currency exchange contracts are creditworthy commercial banks, which minimizes the risk of counterparty nonperformance.

As of March 31, 2021, we had no open forward foreign currency exchange contracts.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

As required by Rule 13a-15(b) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), our management, under the supervision and with the participation of our principal executive officer and principal accounting and financial officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of March 31, 2021. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on such evaluation, our principal executive officer and principal accounting and financial officer have concluded that, as of March 31, 2021, our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended March 31, 2021, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

We have not experienced any material impact to our internal controls over financial reporting, despite the fact that most of our employees are working remotely due to the COVID-19 pandemic. We are continually monitoring and assessing the COVID-19 situation to minimize the impact on the design and operating effectiveness of our internal controls over financial reporting.

Inherent Limitations on Effectiveness of Controls

Internal control over financial reporting has inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements will not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. As of March 31, 2021, there is no litigation pending that would reasonably be expected to have a material adverse effect on our results of operations and financial condition, and no contingent liabilities were accrued as of March 31, 2021.

ITEM 1A. RISK FACTORS

Our business involves significant risks, some of which are described below. You should carefully consider these risks, as well as other information in this Quarterly Report on Form 10-Q, including our condensed financial statements and the notes thereto and "Management's Discussion and Analysis of Financial Condition and Results of Operations." The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations, cash flows, the trading price of our common stock and our growth prospects. Many of the following risks and uncertainties are, and will be, exacerbated by the COVID-19 pandemic *and any worsening of the global business and economic environment as a result. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.*

Summary of Principal Risks Related to Our Business

- We are substantially dependent on the success of our lead product candidate, tenapanor, which may not receive regulatory approval for the control of serum phosphorus in adult patients with CKD on dialysis or for any other related indication, and if approved, may not be successfully commercialized for such indication. On April 29, 2021, the U.S. Food and Drug Administration ("FDA") determined that a submission we made in response to an information request from the FDA constituted a major amendment to our New Drug Application ("NDA") for tenapanor for the control of serum phosphorus, resulting in a three-month extension of the PDUFA date to July 29, 2021. The FDA's information request included a request for additional analyses of our clinical data. The FDA may act on our application by issuing either an approval letter or a Complete Response Letter ("CRL."). Should we wish to pursue our application after receiving a CRL, we may, if possible, resubmit the application with information that addresses the questions or issues identified by the FDA in order to support approval. Resubmissions are subject to review period targets, which vary depending on the underlying submission type and the content of the resubmission.

- Even if we are successful in obtaining regulatory approval for tenapanor for the control of serum phosphorus or for any other related indication, and tenapanor is ultimately commercialized for any approved indications, tenapanor may never achieve market acceptance, sufficient third-party coverage or reimbursement, or commercial success, which will depend, in part, upon the degree of acceptance among physicians, patients, patient advocacy groups, health care payors and the medical community. Additionally, if the number of patients in the market for tenapanor for the approved indication or the price that the market can bear is not as significant as we estimate, or if we are not able to secure adequate coverage and reimbursement for tenapanor, we may not generate sufficient revenue from sales of tenapanor.

- Third-party payor coverage and reimbursement status of newly-approved products are uncertain. Failure to obtain or maintain adequate coverage and reimbursement for tenapanor, if approved, could limit our ability to market tenapanor for the approved indication and decrease our ability to generate revenue. For example, certain policies of the Biden

administration with respect to drug pricing or reimbursement may impact our business and industry. While there is significant uncertainty related to the insurance coverage and reimbursement of newly approved products in general in the United States, there is additional uncertainty related to insurance coverage and reimbursement for drugs, like tenapanor, which, if approved, will be marketed for the approved indication for adult patients with CKD on dialysis. If we are successful in obtaining regulatory approval to market tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for any other related indication, our ability to generate and sustain future revenues from sales of tenapanor for such indication, may be dependent upon whether and when tenapanor, along with other oral end-stage renal disease ("ESRD") related drugs without an injectable or intravenous equivalent, are bundled into the ESRD prospective payment system, and the manner in which such introduction into the ESRD prospective payment system may occur.

- We have hired sales and marketing leadership and employees with technical expertise, and we are required to train, retain and incentivize those sales and marketing personnel. The FDA has extended our PDUFA date to July 29, 2021, and there can be no assurances that we will be successful in retaining our sales and marketing leadership or other key employees necessary for commercial launch throughout this extension, or that we will be able to replace any such leadership or other sales personnel that may leave the Company. Retaining and incentivizing our commercial personnel throughout our extended PDUFA date and thereafter will continue to be expensive and time consuming.

- We rely completely on third parties to manufacture tenapanor and our other product candidates. If they are unable to comply with applicable regulatory requirements, unable to source sufficient raw materials, experience manufacturing or distribution difficulties or are otherwise unable to manufacture sufficient quantities to meet demand, our commercialization of tenapanor, if approved, and our development efforts for tenapanor, RDX013 and our other product candidates may be materially harmed.

- We have a limited operating history, have incurred significant losses since our inception and will incur losses in the future, which makes it difficult for us to assess our future viability.

- We have never generated any revenue from product sales and may never be profitable. Our ability to generate future revenue from product sales or pursuant to milestone payments is dependent upon many factors, including, but not limited to, obtaining regulatory approvals for tenapanor for the control of serum phosphorus or for any other related indication, and establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate supply of product to support the market demand for tenapanor; and obtaining market acceptance of tenapanor as a viable treatment option for the indications for which it is approved and commercialized.

- We will require substantial additional financing to achieve our goals, and the inability to access this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our pre-commercialization efforts for tenapanor and our other product development and platform development activities

- We may not be successful in our efforts to develop RDX013 or expand our pipeline of product candidates, as a result of numerous factors, which may include the inability to access capital necessary to fund such efforts on acceptable terms.

- We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources.

- The COVID-19 pandemic continues to rapidly evolve. The extent to which the pandemic may impact our business, manufacturing, preclinical development activities, preclinical studies, planned and ongoing clinical trials, as well as regulators' review of applications will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as, the duration of the pandemic, travel restrictions and actions to contain the pandemic or treat its impact, such as social distancing, quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. Specifically, while our Phase 3 clinical development of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication is complete, we have ongoing and planned clinical trials for tenapanor or may be required to conduct additional clinical trials, that may be delayed as a result of the restrictions placed on access to dialysis centers during the COVID-19 pandemic or regulators' review of our applications.

Other potential impacts of the COVID-19 pandemic on our various clinical trials, including our ongoing Phase 2 clinical trial for RDX013, include delays or difficulties in any planned clinical site initiation, including difficulties in obtaining Institutional Review Board approvals, recruiting clinical site investigators and clinical site staff, delays or difficulties in enrolling patients, interruption of planned key clinical trial activities, such as clinical trial site data monitoring due to diversion of resources at clinical sites or limitation on travel imposed by federal or state governments.

- Our operating activities may be restricted as a result of covenants related to the indebtedness under our loan and security agreement and we may be required to repay the outstanding indebtedness in an event of default, which could have a materially adverse effect on our business.

- Our products or product candidates may cause undesirable side effects or have other properties that could delay our clinical trials, or delay or prevent regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any regulatory approval that is achieved. If we or others identify undesirable side effects caused by any product candidate following receipt of marketing approval, the ability for us or a collaboration partner to achieve or maintain market acceptance of the approved product could be materially affected and could result in the loss of significant revenue to us, which would materially and adversely affect our results of operations and business.

- The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, including tenapanor for the control of serum phosphorus, or any related indication, our business will be substantially harmed. Even if we receive regulatory approval for a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, any product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Principal Risks Related to Our Business

We are substantially dependent on the success of our lead product candidate, tenapanor, which may not receive regulatory approval for the control of serum phosphorus or for any other related indication or be successfully commercialized for hyperphosphatemia or IBS-C.

To date, we have invested a significant amount of our efforts and financial resources in the research and development of tenapanor, which is currently our lead product candidate. The commercial success of tenapanor will depend on a number of factors, including whether tenapanor's safety and efficacy profile is satisfactory to the FDA and foreign regulatory authorities to gain marketing approval for the control of serum phosphorus, or any other related indication. On April 29, 2021, the FDA determined that a submission we made in response to an information request from the FDA constituted a major amendment to our NDA, resulting in a three-month extension of the PDUFA date to July 29, 2021. The FDA's information request included a request for additional analyses of our clinical data. The FDA may act on our application by issuing an approval letter or a CRL. Should we wish to pursue an application after receiving a CRL, we may, if possible, resubmit the application with information that addresses the questions or issues identified by the FDA in order to support approval. Resubmissions are subject to review period targets, which vary depending on the underlying submission type, the content of the resubmission and regulators' ability to conduct the review. If we are successful in obtaining approval for tenapanor for the control of serum phosphorus, or for a related indication, the commercial success of tenapanor will depend on a number of additional factors, including the following:

- the ability of the third-party manufacturers we contract with to provide an adequate (in amount and quality) supply of product to support the market demand for tenapanor for the treatment of IBS-C, and/or if approved, tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication, particularly in light of the effects of the COVID-19 pandemic;

- whether or not the content and breadth of the label approved by the FDA or foreign regulatory authorities may materially and adversely impact our ability or the ability of our collaboration partners to commercialize the product for the approved indication, or for any other indication;

- whether we will be required to conduct clinical trials in addition to those anticipated to obtain regulatory approval or adequate commercial pricing;

- the prevalence and severity of adverse side effects of tenapanor;

- the timely receipt of necessary marketing approvals from the FDA and foreign regulatory authorities;

- our ability, either alone, or with a collaboration partner, to successfully commercialize tenapanor, if approved for marketing and sale by the FDA or foreign regulatory authorities, including educating physicians and patients about the benefits, administration and use of tenapanor;
- achieving and maintaining compliance with all regulatory requirements applicable to tenapanor;
- acceptance of tenapanor as safe, effective and well-tolerated by patients and the medical community;
- our ability, alone or with collaboration partners, to manage the complex pricing and reimbursement negotiations associated with marketing the same product at different doses for separate indications for tenapanor for the treatment of IBS-C, and, if approved, for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of tenapanor compared to alternative and competing treatments;
- obtaining and sustaining an adequate level of coverage and reimbursement for tenapanor by third-party payors;
- enforcing intellectual property rights in and to tenapanor;
- avoiding third-party interference, opposition, derivation or similar proceedings with respect to our patent rights, and avoiding other challenges to our patent rights and patent infringement claims; and
- a continued acceptable safety and tolerability profile of tenapanor following approval.

As tenapanor is a first-in-class drug, there is a higher likelihood that approval may not be attained as compared to a class of drugs with approved products. Although tenapanor met the primary endpoints in all of the three Phase 3 clinical trials evaluating tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis, the FDA requested additional analyses of the clinical data submitted in our NDA in order to more fully evaluate our clinical data, including as compared to approved therapies. The submission of the new analyses was determined to be a major amendment to our NDA, and resulted in a three month extension of our PDUFA date. There can be no assurances that we will receive regulatory approval to market tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for any other related indication. The FDA, after consideration of our submission may issue a CRL. Further, it may not be possible or practicable to demonstrate, or if approved, to market tenapanor on the basis of certain of the benefits we believe tenapanor possesses. If the number of patients in the market for tenapanor based on the approved indication or the price that the market can bear is not as significant as we estimate, or if we are not able to secure adequate coverage and reimbursement for tenapanor, we may not generate sufficient revenue from sales of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for any other related indication, if approved, or for IBS-C if commercialized. There can be no assurance that tenapanor will ever be successfully commercialized or that we will ever generate income from sales of tenapanor. If we are not successful in obtaining approval for tenapanor for the control of serum phosphorus or for any other related indication, or we are not successful in commercializing tenapanor, or are significantly delayed in doing so, our business will be materially harmed.

Even if we are successful in obtaining regulatory approval for tenapanor for the control of serum phosphorus or for any other related indication, and tenapanor is ultimately commercialized for any approved indications, tenapanor may never achieve market acceptance, sufficient third-party coverage or reimbursement, or commercial success, which will depend, in part, upon the degree of acceptance among physicians, patients, patient advocacy groups, health care payors and the medical community.

Market acceptance of tenapanor for IBS-C and, in the event that marketing approval is obtained, for the control of serum phosphorus or for another other related indication, depends on a number of factors, including:

- the breadth and content of the approved label, and the clinical indications for which it is approved;
- the efficacy demonstrated in our clinical trials;
- with respect to tenapanor for the control of serum phosphorus or for another other related indication, whether tenapanor, along with other oral only medications, are included in the bundled prospective payment system for the treatment of ESRD patients, and the time and manner in which such transition is achieved;

- the prevalence and severity of any side effects and overall safety and tolerability profile of the product;
- advantages over new or traditional or existing therapies, including recently approved therapies or therapies that the physician community anticipate will be approved;
- acceptance by physicians, major operators of clinics and patients of tenapanor as a safe, effective and well-tolerated treatment;
- relative convenience and ease of administration of tenapanor;
- the potential and perceived advantages of tenapanor over current treatment options or alternative treatments, including future alternative treatments;
- the cost of treatment in relation to alternative treatments and the willingness to pay for tenapanor, if approved, on the part of physicians and patients;
- the availability of alternative products and their ability to meet market demand; and
- the quality of our relationships with patient advocacy groups.

Any failure of tenapanor to achieve market acceptance, sufficient third-party coverage or reimbursement, or commercial success for any approved indications would adversely affect our results of operations.

If we are not able to retain our sales and marketing leadership and other key employees during the extended PDUFA date, and we are not able to replace any lost personnel we may not be able to commercialize tenapanor or any of our other product candidates.

If approved, we currently plan to commercialize tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another related indication, on our own. We have hired sales leadership and sales employees with technical expertise, and we are required to train, retain and incentivize those sales personnel. The FDA has extended our PDUFA date to July 29, 2021, and there can be no assurances that we will be successful in retaining our sales and marketing leadership or other key employees necessary for commercial launch throughout this extension, or that we will be able to replace any such leadership or other sales personnel that may leave the Company. Retaining and incentivizing our commercial personnel throughout our extended PDUFA date and thereafter will continue to be expensive and time consuming. Even if we are able to retain our key sales and marketing leadership during this extended PDUFA date, and tenapanor is approved for the control of serum phosphorus in adult patients with CKD on dialysis, or any related indication, as a company, we have no prior experience in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in managing and retaining a sales organization, including our ability to secure the capital necessary to fund such efforts on acceptable terms, provide adequate training to sales and marketing personnel, comply with regulatory requirements applicable to the marketing and sale of drug products and effectively manage a geographically dispersed sales and marketing team.

If we fail to maintain or replace our internal sales, marketing and distribution capabilities, we may need to delay the commercialization of tenapanor for the control of serum phosphorus or for another other related indication, if approved, or such commercialization could be adversely impacted.

Third-party payor coverage and reimbursement status of newly-approved products are uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our products, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The pricing, coverage and reimbursement of our product candidates, if approved, must be adequate to support a commercial infrastructure. The availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to be able to afford treatments such as ours, assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other third-party payors. If coverage and reimbursement are not available, or are available only to limited levels, we, or our collaboration partners, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by the Centers for Medicare & Medicaid Services ("CMS"), an agency within the United States Department of Health and Human Services responsible for administering the Medicare program, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for products such as ours.

There is increased uncertainty related to insurance coverage and reimbursement for drugs, like tenapanor, which, if approved, will be marketed for the control of serum phosphorus in CKD patients on dialysis or for another other related indication. In January 2011, CMS implemented a new prospective payment system for dialysis treatment. Under the ESRD prospective payment system, CMS generally makes a single bundled payment to the dialysis facility for each dialysis treatment that covers all items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home, including the cost of certain routine drugs. The inclusion of oral medications without injectable or intravenous equivalents in the bundled payment was initially delayed until January 1, 2014 and through several subsequent legislative actions was delayed until January 1, 2025. As a result, absent further legislation or regulation on this matter, beginning in 2025, oral ESRD-related drugs without injectable or intravenous equivalents may be included in the ESRD bundle and separate Medicare payment for these drugs will no longer be available, as is the case today under Medicare Part D. While it is too early to project the full impact that bundling may have on tenapanor and our business should tenapanor be brought into the bundle in 2025, or at any time, we may be unable to sell tenapanor, if approved, to dialysis providers on a profitable basis if third-party payors reduce their current levels of payment, or if our costs of production are higher than levels necessary for an appropriate gross margin after payment of all discounts, rebates and chargebacks.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, Japan, China and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, these caps may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

We rely completely on third parties to manufacture tenapanor and our other product candidates. If they are unable to comply with applicable regulatory requirements, unable to source sufficient raw materials, experience manufacturing or distribution difficulties or are otherwise unable to manufacture sufficient quantities to meet demand, our commercialization of tenapanor, if approved, and our development efforts for tenapanor, RDX013 and our other product candidates may be materially harmed.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture tenapanor or any of other our product candidates on a commercial scale, or to manufacture our drug supplies for use in the conduct of our nonclinical and clinical studies. The facilities used by our contract manufacturers to manufacture our drug supply are subject to inspection by the FDA. Our ability to control the manufacturing process of our product candidates is limited to the contractual requirements and obligations we impose on our contract manufacturer. Although they are contractually required to so do, we are completely dependent on our contract manufacturing partners for compliance with the regulatory requirements, known as current Good Manufacturing Practice requirements ("cGMPs"), for manufacture of both active drug substances and finished drug products.

The manufacture of pharmaceutical products requires significant expertise and capital investment. Manufacturers of pharmaceutical products often encounter difficulties in commercial production. These problems may include difficulties with production costs and yields, quality control, including stability of the product and quality assurance testing, and shortages of qualified personnel, as well as compliance with federal, state and foreign regulations and the challenges associated with complex supply chain management. Even if our contract manufacturers do not experience problems and commercial

manufacturing is achieved, their maximum or available manufacturing capacities may be insufficient to meet commercial demand. Finding alternative manufacturers or adding additional manufacturers requires a significant amount of time and involves significant expense. New manufacturers would need to develop and implement the necessary production techniques and processes, which along with their facilities, would need to be inspected and approved by the regulatory authorities in each applicable territory. In addition, the raw materials necessary to make API for our products are acquired from a limited number of sources. Any delay or disruption in the availability of these raw materials could result in production disruptions, delays or higher costs with consequent adverse effects on us.

If our contract manufacturers fail to adhere to applicable GMP or other regulatory requirements, experience delays or disruptions in the availability of raw materials or experience manufacturing or distribution problems, we may suffer significant consequences, including the inability to meet our product requirements for our clinical development programs, and if tenapanor is approved for marketing for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication, such events could result in product seizures or recalls, loss of product approval, fines and sanctions, reputational damage, shipment delays, inventory shortages, inventory write-offs and other product-related charges and increased manufacturing costs. As a result, or if maximum or available manufacturing capacities are insufficient to meet demand, our development or our commercialization efforts for tenapanor for the control of serum phosphorus or for another other related indication, if approved, may be materially harmed.

Risks Related to our Financial Condition and Capital Requirements

We have a limited operating history, have incurred significant losses since our inception and we will incur losses in the future, which makes it difficult to assess our future viability.

We are a clinical-stage biopharmaceutical company with a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused substantially all of our efforts on our research and development activities, including developing tenapanor and developing our proprietary drug discovery and design platform. To date, we have not commercialized any products or generated any revenue from the sale of products.

We are not profitable and have incurred losses in each year since our inception in October 2007, and we do not know whether or when we will become profitable. We continue to incur significant research, development and other expenses related to our ongoing operations. As of March 31, 2021, we had an accumulated deficit of $587.9 million.

We expect to continue to incur substantial operating losses for the foreseeable future as we prepare for the potential commercialization of, and incur manufacturing and development costs for, tenapanor for the control of serum phosphorus in CKD patients on dialysis or for another other related indication; as we commence commercialization of tenapanor for that or another related indication, if approved; as we incur development costs for RDX013; and as we continue our discovery and research activities.

Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Further, the net losses we incur may fluctuate significantly from quarter-to-quarter and year-to-year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We have substantial net operating loss and tax credit carryforwards for Federal and California income tax purposes. Such net operating losses and tax credits carryforwards may be reduced as a result of certain intercompany restructuring transactions. In addition, the future utilization of such net operating loss and tax credit carryforwards and credits will be subject to limitations, pursuant to Internal Revenue Code Sections 382 and 383, as a result of ownership changes that have occurred previously and additional limitations may be applicable as a result of ownership changes that could occur in the future.

We have never generated any revenue from product sales and may never be profitable.

We received FDA approval for our NDA for tenapanor for the treatment of IBS-C in adults in September 2019. However, we have not commercialized tenapanor for IBS-C ourselves in the United States and have not entered into a collaboration partnership for such commercialization. We have no other products approved for sale and have never generated any revenue from product sales. On April 29, 2021, the FDA determined that a submission we made in response to an information request from the FDA related to our NDA for the control of serum phosphorus in adult patients with CKD on dialysis constituted a major amendment to our NDA, resulting in a three-month extension of the PDUFA date to July 29, 2021. The FDA's information request included a request for additional analyses of our clinical data. The FDA may act on our application by

either issuing an approval letter or a CRL. Should we wish to pursue an application after receiving a CRL, we may, if possible, resubmit the application with information that addresses the questions or issues identified by the FDA in order to support approval. Resubmissions are subject to review period targets, which vary depending on the underlying submission type and the content of the resubmission. There can be no assurances that our NDA for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis will be approved for such indication or any other related indication. Our ability to generate revenue from product sales and achieve profitability depends on our ability to obtain such approval by the FDA and the ability of our collaboration partners to obtain regulatory approval to market tenapanor in their respective territories. There can be no assurances that we will generate product revenue from sales of tenapanor, either on our own, or with a collaboration partner. Our ability to generate future revenue from product sales or pursuant to milestone payments depends heavily on many factors, including but not limited to:

- obtaining regulatory approvals for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication, either on our own or with one or more collaboration partners;

- our ability to successfully commercialize tenapanor, which has been approved by the FDA for the treatment of IBS-C in adults, and/or tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication, if approved, either on our own or with one or more collaboration partners;

- establishing and maintaining supply and manufacturing relationships with third parties that can provide an adequate (in amount and quality) supply of product to support the market demand for tenapanor for the treatment of IBS-C, and/or, if approved, tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication;

- obtaining market acceptance of tenapanor as a viable treatment option for the indications for which it is approved and commercialized;

- addressing any competing technological and market developments;

- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how, and our ability to develop, manufacture and commercialize our product candidates and products without infringing intellectual property rights of others; and

- attracting, hiring, and retaining qualified personnel.

In cases where we are successful in obtaining regulatory approvals to market tenapanor for one or more indications, our revenue will be dependent, in part, upon the size of the markets in the territories for which regulatory approval is granted, the breadth of the indication and the label for which approval is granted, accepted price for the product, the ability to get reimbursement at any price and whether we are commercializing the product or the product is being commercialized by a collaboration partner, and in such case, whether we have royalty and/or co-promotion rights for that territory, and whether any royalty we have a right to receive from a collaboration partner is in excess of the royalty we owe AstraZeneca as a result of the termination of our License Agreement with AstraZeneca in 2015. See Note 12, Collaboration and Licensing Agreements, in the notes to our financial statements, included in Part II, Item 8, for details on our obligations to AstraZeneca. While there is significant uncertainty related to the insurance coverage and reimbursement of newly approved products in general in the United States, there is additional uncertainty related to insurance coverage and reimbursement for drugs, like tenapanor, which, if approved, will be marketed for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication. If we are successful in obtaining regulatory approval to market tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication, our ability to generate and sustain future revenues from sales of tenapanor for such indication, may be dependent upon whether and when tenapanor, along with other oral end-stage renal disease (“ESRD”) related drugs without an injectable or intravenous equivalent, are bundled into the ESRD prospective payment system, and the manner in which such introduction into the ESRD prospective payment system may occur. See “Third-party payor coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our products, if approved, could limit our ability to market those products and decrease our ability to generate revenue” below. Additionally, if the number of patients for the approved indication suitable for tenapanor is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, coverage and reimbursement for tenapanor are not available in the manner and to the extent which we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from the sale of tenapanor, even if approved. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to generate revenue from product sales would likely depress our market value and could impair our ability to raise capital, expand our business,

discover or develop other product candidates or continue our operations. A decline in the value of our common stock could cause our stockholders to lose all or part of their investment.

We will require substantial additional financing to achieve our goals, and the inability to access this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our commercialization efforts for tenapanor for the control of serum phosphorus or for another other related indication, if approved, and our other product development and platform development activities.

Since our inception, most of our resources have been dedicated to our research and development activities, including developing our clinical product candidate tenapanor and developing our proprietary drug discovery and design platform. We believe that we will continue to expend substantial resources for the foreseeable future, including, if approved, costs associated with the commercialization of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication, research and development, conducting preclinical studies and clinical trials for our other programs, including RDX013, obtaining regulatory approvals, scaling our manufacturing processes for our product candidates and sales and marketing. Because the outcome of any clinical trial and/or regulatory approval process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization or co-promotion of any of our product candidates. Our future funding requirements will depend on many factors, including, but not limited to:

- the FDA's actions and decisions with respect to the NDA submitted to the FDA on June 30, 2020 to request marketing authorization for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis, including the FDA's actions after the three-month extension of the PDUFA date to July 29, 2021;
- our ability to successfully commercialize tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication, if approved, either alone or with one or more collaboration partners;
- the sales price and the availability of adequate third-party reimbursement for tenapanor, if approved;
- the manufacturing costs of our product candidates, and the availability of one or more suppliers for our product candidates at reasonable costs, both for clinical and commercial supply;
- the selling and marketing costs associated with tenapanor, including the cost and timing of maintaining our sales and marketing capabilities;
- our ability to maintain our existing collaboration partnerships and to establish additional collaboration partnerships, in-license/out-license, joint ventures or other similar arrangements and the financial terms of such agreements;
- the timing, receipt, and amount of sales of, or royalties on, tenapanor, if any;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the number and scope of preclinical and discovery programs that we decide to pursue or initiate, and any clinical trials we decide to pursue for other product candidates, including RDX013;
- the time and cost necessary to respond to technological and market developments;
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of tenapanor or any of our product candidates; and
- the payment of interest and principal related to our loan and security agreement entered into with Solar Capital and Western Alliance Bank in May 2018, as amended in October 2020, March 2021 and May 2021.

Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our research activities, preclinical and clinical trials for our product candidates and our establishment and maintenance of sales and marketing capabilities or other activities that may be necessary to commercialize tenapanor, either alone or with collaboration partners. Additionally, our inability to access capital on a timely basis and on terms that are acceptable to us may force us to restructure

certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the development or commercialization of tenapanor or certain of our product candidates through the use of alternative structures.

Our operating activities may be restricted as a result of covenants related to the indebtedness under our loan and security agreement and we may be required to repay the outstanding indebtedness in an event of default, which could have a materially adverse effect on our business.

On May 16, 2018, we entered into a loan and security agreement with Solar Capital, Ltd. and Western Alliance Bank (collectively, the "Lenders") pursuant to which the Lenders agreed to provide us a $50.0 million term loan facility with a maturity date of November 1, 2022. On October 9, 2020, we entered into an amendment to the loan and security agreement. The full amount of the loan was funded on May 16, 2018. Until we have repaid such indebtedness, the loan and security agreement subjects us to various customary covenants, including requirements as to financial reporting and insurance and restrictions on our ability to dispose of our business or property, to change our line of business, to liquidate or dissolve, to enter into any change in control transaction, to merge or consolidate with any other entity or to acquire all or substantially all the capital stock or property of another entity, to incur additional indebtedness, to incur liens on our property, to pay any dividends or other distributions on capital stock other than dividends payable solely in capital stock, to redeem capital stock, to enter into licensing agreements, to engage in transactions with affiliates, and to encumber our intellectual property. Our business may be adversely affected by these restrictions on our ability to operate our business.

We are permitted to make interest only payments on the loan facility through December 1, 2021, unless we have not received FDA approval for our NDA for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis on or before July 31, 2021, or the FDA issues a complete response letter in connection with such NDA. In either event, the period in which we are permitted to make interest only payments shall end on the earlier of June 1, 2021, or the first day of the month following the date that the FDA issues a CRL. However, we may be required to repay the outstanding indebtedness under the loan facility if an event of default occurs under the loan and security agreement. An event of default will occur if, among other things, we fail to make payments under the loan and security agreement; we breach any of our covenants under the loan and security agreement, subject to specified cure periods with respect to certain breaches; the Lenders determine that a material adverse change has occurred; we or our assets become subject to certain legal proceedings, such as bankruptcy proceedings; we are unable to pay our debts as they become due; or we default on contracts with third parties which would permit the Lenders to accelerate the maturity of such indebtedness or that could have a material adverse change on us. We may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time any such event of default occurs. In this case, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant to others' rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. The Lenders could also exercise their rights as collateral agent to take possession of and to dispose of the collateral securing the term loans, which collateral includes substantially all of our property (excluding intellectual property, which is subject to a negative pledge). Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events.

Additional Risks Related to Our Business and Industry

We may not be successful in our efforts to develop RDX013 or any other product candidates that are at an early stage of development, or expand our pipeline of product candidates, as a result of numerous factors, which may include the inability to access capital necessary to fund such efforts on acceptable terms.

A key element of our strategy has been focused on the expansion of our pipeline of product candidates utilizing our proprietary drug discovery and design platform and to advance such product candidates through clinical development. Our inability to access capital in a timely manner or on acceptable terms to fund our early stage product candidates may force us to consider certain restructuring activities to enable the funding of those early assets through the use of alternative structures. In addition, of the large number of drugs in development, only a small percentage of such drugs successfully complete the FDA regulatory approval process and are commercialized. Accordingly, even if we are able to continue to fund our research and early-stage development programs, there can be no assurance that any product candidates will reach the clinic or be successfully developed or commercialized.

Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Although our research and development efforts to date have resulted in several development programs, we may not be able to develop product candidates that are safe, effective and well-tolerated. Our research programs may initially show promise in identifying potential product candidates, and we may select candidates for development, yet we may fail to advance product candidates to clinical development for many reasons, including the following:

- we may be unable to access sufficient capital on acceptable terms to fund the development of all of our assets and as a result we may be forced to delay or terminate the development of certain product candidates, or to consider restructuring efforts to secure alternate funding for those assets;
- the research methodology used and our drug discovery and design platform may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer reasonable;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective, well-tolerated or otherwise does not meet applicable regulatory or commercial criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe, effective and well-tolerated by patients, the medical community or third-party payors, if applicable.

Even if we are successful in continuing to expand our pipeline, through our own research and development efforts, the potential product candidates that we identify or for which we acquire rights may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize a product pipeline, we may not be able to generate revenue from product sales in future periods or ever achieve profitability.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome and the results of earlier studies and trials may not be predictive of future trial results.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical and clinical studies of our product candidates, including RDX013, may not be predictive of the results of later-stage clinical trials. An unexpected adverse event profile, or the results of drug-drug interaction studies, may present challenges for the future development and commercialization of a product candidate for a particular condition despite receipt of positive efficacy data in a clinical study. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials for similar indications that we are pursuing due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks.

Our ongoing RDX013 Phase 2 clinical trial or any of our other ongoing clinical trials may be impacted by the COVID-19 pandemic in a number of ways, including delays or difficulties in any planned clinical site initiation, difficulties in obtaining IRB approvals, recruiting clinical site investigators and clinical site staff, delays or difficulties in enrolling patients, interruption of planned key clinical trial activities, such as clinical trial site data monitoring due to diversion of resources at clinical sites or limitation on travel imposed by federal or state governments.

Furthermore, we could encounter delays if our ongoing RDX013 Phase 2 clinical trial, or any other of our clinical trials are suspended or terminated by us, by the IRBs of the institutions in which the trial is being conducted, or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

In addition, identifying and qualifying patients to participate in our RDX013 Phase 2 clinical trial or any of our other clinical trials is critical to our success. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in testing our product candidates. Patients may be unwilling to participate in our clinical studies because

of concerns about adverse events observed with the current standard of care, competitor products and/or other investigational agents, in each case for the same indications and/or similar patient populations. In addition, patients currently receiving treatment with the current standard of care or a competitor product may be reluctant to participate in a clinical trial with an investigational drug, or our inclusion and exclusion criteria for our clinical trials may present challenges in identifying acceptable patients. As a result, the timeline for recruiting patients and conducting our RDX013 Phase 2 clinical trial or any of our other clinical trials may be delayed. These delays could result in increased costs, delays in advancing our development of our product candidates, or termination of the clinical studies altogether. Any of these occurrences may significantly harm our business, financial condition and prospects.

Furthermore, even though we have completed our Phase 3 clinical development program for tenapanor for the control of serum phosphorus, the results may not be sufficient to obtain the desired regulatory approval for tenapanor, or if such regulatory approval is obtained, the content of the label approved by regulatory authorities may materially and adversely impact our ability to commercialize the product for the approved indication.

We rely on third parties to conduct some of our nonclinical studies and all of our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for additional products or commercialize our product candidates.

We do not have the ability to independently conduct clinical trials and, in some cases, nonclinical studies. We rely on medical institutions, clinical investigators, contract laboratories, and other third parties, such as CROs, to conduct clinical trials on our product candidates. The third parties with whom we contract for execution of the clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these third parties are not our employees, and except for contractual duties and obligations, we control only certain aspects of their activities and have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely, and will continue to rely, on these third parties to conduct some of our nonclinical studies and all of our clinical trials, we remain responsible for ensuring that each of our studies and clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on third parties does not relieve us of our regulatory responsibilities. We, and these third parties are required to comply with current GLPs for nonclinical studies, and good clinical practices (“GCPs”) for clinical studies. GLPs and GCPs are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area (“EEA”) and comparable foreign regulatory authorities for all of our products in nonclinical and clinical development, respectively. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party contractors fail to comply with applicable regulatory requirements, including GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the European Medicines Agency (“EMA”), or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Our products or product candidates may cause undesirable side effects or have other properties that could delay our clinical trials, or delay or prevent regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any regulatory approval that is achieved. If we or others identify undesirable side effects caused by any product candidate following receipt of marketing approval, the ability to market such product candidate could be compromised.

Undesirable side effects caused by our products or product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials, result in the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities or limit the commercial profile of an approved label. To date, patients treated with tenapanor have experienced drug-related side effects including diarrhea, nausea, vomiting, flatulence, abdominal discomfort, abdominal pain, abdominal distention and changes in electrolytes. Despite our receipt of marketing approval for tenapanor for IBS-C in adults and the completion of our Phase 3 clinical program for tenapanor for the control of serum phosphorus, in the event that future trials conducted by us with tenapanor, or trials we conduct with RDX013 or our other product candidates, reveal an unacceptable severity and prevalence of these or other side effects, such trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of tenapanor, RDX013, or any such other product candidate, for any or all targeted indications. Additionally, despite a positive efficacy profile, the prevalence and/or severity of these or other side effects could cause us to cease further development of a product candidate for a particular indication, or entirely. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, if we or others identify undesirable side effects caused by one of our products for which we have received regulatory approval, a number of potentially significant negative consequences could occur, including:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we or a collaboration partner may be required to recall the product;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof, including the imposition of a Risk Evaluation and Mitigation Strategy ("REMS") which could require creation of a Medication Guide or patient package insert outlining the risks of such side effects for distribution to patients, a communication plan to educate healthcare providers of the drugs' risks, as well as other elements to assure safe use of the product, such as a patient registry and training and certification of prescribers;
- we or a collaboration partner may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us, or a collaboration partner, from achieving or maintaining market acceptance of a particular product candidate, if approved, and could result in the loss of significant revenue to us, which would materially and adversely affect our results of operations and business.

We face substantial competition and our competitors may discover, develop or commercialize products faster or more successfully than us.

The biotechnology and pharmaceutical industries are highly competitive, and we face significant competition from companies in the biotechnology, pharmaceutical and other related markets that are researching and marketing products designed to address diseases that we are currently developing products to treat. If approved for marketing by the FDA or other regulatory agencies, tenapanor, as well as our other product candidates, would compete against existing treatments.

For example, tenapanor, if approved for the control of serum phosphorus in adult patients with CKD on dialysis or for another related indication, will compete with phosphate binders used for the same or similar indication`. If approved, our label for tenapanor for the control of serum phosphorus may include data comparing the effectiveness of tenapanor to phosphate binders used for the same indication. The various types of phosphate binders commercialized in the United States include the following:

- Calcium carbonate (many over-the-counter brands including Tums and Caltrate);
- Calcium acetate (several prescription brands including PhosLo and Phoslyra);
- Lanthanum carbonate (Fosrenol);
- Sevelamer hydrochloride (Renagel);
- Sevelamer carbonate (Renvela);
- Sucroferric oxyhydroxide (Velphoro); and
- Ferric citrate (Auryxia).

All of the phosphate binders listed above are available as generics in the U.S., with the exception of Velphoro and Auryxia. In addition to the currently available phosphate binders, we are aware of at least two other binders in development, including fermagate (Alpharen), an iron-based binder in Phase 3 being developed by Opko Health, Inc., and PT20, an iron-based binder in Phase 3 being developed by Shield Therapeutics.

In respect of tenapanor for the treatment of IBS-C, numerous treatments exist for constipation and the constipation component of IBS-C, many of which are over-the-counter. These include psyllium husk (such as Metamucil), methylcellulose (such as Citrucel), calcium polycarbophil (such as FiberCon), lactulose (such as Cephulac), polyethylene glycol (such as MiraLax), sennosides (such as Exlax), bisacodyl (such as Ducolax), docusate sodium (such as Colace), magnesium hydroxide (such as Milk of Magnesia), saline enemas (such as Fleet) and sorbitol. These agents are generally inexpensive and work well to temporarily relieve constipation.

We are aware of four prescription products marketed for certain patients with IBS-C, including Linzess (linaclotide), Amitiza (lubiprostone), Trulance (plecanatide) and Zelnorm (tegaserod maleate).

It is possible that our competitors' drugs may be less expensive and more effective than our product candidates, or that will render our product candidates obsolete. It is also possible that our competitors will commercialize competing drugs or treatments before we or our collaboration partners can launch any products developed from our product candidates. We also anticipate that we will face increased competition in the future as new companies enter into our target markets.

Many of our competitors have materially greater name recognition and financial, manufacturing, marketing, research and drug development resources than we do. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Large pharmaceutical companies in particular have extensive expertise in preclinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies, and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaboration partnerships or licensing relationships with our competitors.

We may experience difficulties in managing our current activities and growth given our level of managerial, operational, financial and other resources.

While we have continued to work to optimize our management composition, personnel and systems to support our current activities for future growth, these resources may not be adequate for this purpose. Our need to effectively execute our business strategy requires that we:

- manage any commercialization activities in which we may engage effectively;
- manage our clinical trials effectively;
- manage our internal research and development efforts effectively while carrying out our contractual obligations to licensors, contractors, collaborators, government agencies and other third parties;
- continue to improve our operational, financial and management controls, reporting systems and procedures; and
- retain and motivate our remaining employees and potentially identify, recruit, and integrate additional employees.

If we are unable to maintain or expand our managerial, operational, financial and other resources to the extent required to manage our development and commercialization activities, our business will be materially adversely affected.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- injury to our reputation;

- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize or co-promote our product candidates.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of any products we develop. Although we maintain product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

If we fail to attract, retain and motivate our executives, senior management and key personnel, our business will suffer.

Recruiting and retaining qualified scientific, clinical, medical, manufacturing, and sales and marketing personnel is critical to our success. We are highly dependent on our executives, senior management and certain other key employees. The loss of the services of our executives, senior management or other key employee could impede the achievement of our research, development and commercial objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executives, senior management and other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain marketing approval of and commercialize products. We may be unable to hire, train or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel, particularly in our geographic regions. If we are unable to continue to attract and retain high quality personnel, our ability to grow and pursue our business strategy will be limited.

Our proprietary drug discovery and design platform, and, in particular, APECCS, is a new approach to the discovery, design and development of new product candidates and may not result in any products of commercial value. Furthermore, the APECCS aspects of our drug discovery and design platform may have diminished relevance to our efforts focused on the discovery of targets and therapies for the treatment of renal diseases.

We have developed a proprietary drug discovery and design platform integrating our proprietary chemistry capabilities and our APECCs stem cell platform to enable the identification, screening, testing, design and development of new product candidates, and have developed APECCS as a component of this of this platform. We have utilized APECCS in the design of our small molecules and to identify new and potentially novel targets in the GI tract. However, there can be no assurance that APECCS will be able to identify new targets in the GI tract or that any of these potential targets or other aspects of our proprietary drug discovery and design platform will yield product candidates that could enter clinical development and, ultimately, be commercially valuable. In addition, as we focus our efforts on the discovery and design of therapies for the treatment of cardiorenal diseases, we may need to further develop our proprietary drug discovery and design platform to enhance its usefulness in the identification, screening, testing, design and development of new product candidates for the treatment of cardiorenal diseases. There can be no assurances that we will be successful in such additional development of our platform or that our platform will yield product candidates for the treatment of renal diseases.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data,

such as information that we may collect in connection with clinical trials in the U.S. and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. In addition, California enacted the California Consumer Privacy Act ("CCPA") on June 28, 2018, which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states. Further, the California Privacy Rights Act (CPRA) recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

In Europe, the European Union General Data Protection Regulation (GDPR) went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the European Economic Area (EEA). Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Relatedly, following the United Kingdom’s withdrawal from the European Economic Area and the European Union, and the expiry of the transition period, companies have to comply with both the GDPR and the GDPR as incorporated into United Kingdom national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection law remains unclear, for example around how data can lawfully be transferred between each jurisdiction, which may expose us to further compliance risk.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, CROs, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

We and our collaborators, CROs and other contractors and consultants depend on information technology systems, and any failure of these systems could harm our business. Security breaches, loss of data, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business, results of operations and financial condition.

We and our collaborators, CROs, and other contractors and consultants collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we and our collaborators, CROs and other contractors and consultants collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we and our collaborators, CROs and other

contractors and consultants do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems to prevent a data compromise, and rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information. Our internal information technology systems and infrastructure, and those of our current and any future collaborators, CROs, contractors and consultants and other third parties on which we rely, are vulnerable to damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization.

The risk of a security breach or disruption or data loss, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs, and/or of our efforts to commercialize tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication, if approved. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws, if applicable, including HIPAA. Moreover, if a computer security breach affects our systems or those of our collaborators, CROs or other contractors, or results in the unauthorized release of personally identifiable information, our reputation could be materially damaged. We would also be exposed to a risk of loss or litigation and potential liability, which could materially adversely affect our business, results of operations and financial condition.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. Even when HIPAA does not apply, according to the Federal Trade Commission (the “FTC”) failing to take appropriate steps to keep consumers’ personnel information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act (the “FTCA”) 15 U.S. C § 45(a). The FTC expects a

company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The FTC's guidance for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule. We may also be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA. For example, California recently enacted legislation the CCPA, which went into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for "protected health information" maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context. Further, the CPRA recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

We have previously identified a material weakness in our internal control over financial reporting. If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us and could have a material adverse effect on the price of our common stock.

In 2019, management and our independent registered public accounting firm identified a control deficiency that constituted a material weakness in our internal control over financial reporting. The material weakness was due to a failure in the design and implementation of controls over the evaluation of the terms of our clinical trial contracts for inclusion into our clinical financial model which estimates clinical trial expenses. Specifically, we had failed to properly interpret an expense in our clinical trial contracts which resulted in the over accrual of our clinical trial expenses during 2018 and the first quarter of 2019.

We developed and implemented a remediation plan for this material weakness which included modifications to the design and implementation of certain internal controls, and the material weakness was remediated as of December 31, 2019. Although we have remediated this material weakness, as attested by our independent registered public accounting firm, we can give no assurance that an additional material weakness or significant deficiency in our internal controls over financial reporting will not be identified in the future. Our failure to implement and maintain effective internal controls over financial reporting could result in errors in our financial statements that could result in a restatement of our financial statements and cause us to fail to meet our reporting obligations. If we cannot in the future favorably assess the effectiveness of our internal controls over financial reporting, investor confidence in the reliability of our financial reports may be adversely affected, which could have a material adverse effect on the trading price of our common stock.

We have formed in the past, and may form in the future, collaboration partnerships, joint ventures and/or licensing arrangements, and we may not realize the benefits of such collaborations.

We have current collaboration partnerships for the commercialization of tenapanor in certain foreign countries, and we may form additional collaboration partnerships, create joint ventures or enter into additional licensing arrangements with third parties in the United States and abroad that we believe will complement or augment our existing business. In particular, we have formed collaboration partnerships with Kyowa Kirin Co., Ltd. ("KKC") for certain research programs and for commercialization of tenapanor for hyperphosphatemia in Japan; with Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd. ("Fosun Pharma") for commercialization of tenapanor for hyperphosphatemia and IBS-C in China and related territories; and in Canada with Knight Therapeutics, Inc. ("Knight") for commercialization of tenapanor for IBS-C and hyperphosphatemia. We face significant competition in seeking appropriate collaboration partners, and the process to identify an appropriate partner and negotiate appropriate terms is time-consuming and complex. Any delays in identifying suitable additional collaboration partners and entering into agreements to develop our product candidates could also delay the

commercialization of our product candidates, which may reduce their competitiveness even if they reach the market. There is no guarantee that our current collaboration partnerships or any such arrangements we enter into in the future will be successful, or that any collaboration partner will commit sufficient resources to the development, regulatory approval, and commercialization effort for such products, or that such alliances will result in us achieving revenues that justify such transactions.

The ongoing COVID-19 pandemic, or any other outbreak of epidemic diseases, or the perception of their effects, could have a material adverse effect on our business, financial condition, results of operations or cash flows.

Outbreaks of epidemic, pandemic, or contagious diseases, such as the current novel coronavirus ("COVID-19") pandemic or, historically, the Ebola virus, Middle East Respiratory Syndrome, Severe Acute Respiratory Syndrome or the H1N1 virus, could disrupt our business. Business disruptions could include disruptions or restrictions on our ability to conduct our clinical trials, as planned, travel, as well as temporary closures of the facilities of our collaboration partners, suppliers or contract manufacturers. Any disruption of our clinical trial operations, collaboration partners, suppliers or contract manufacturers could adversely impact our operating results.

Economic and health conditions related to the COVID-19 pandemic in the United States and across most of the globe remain uncertain and continue to evolve. While at this point, the extent to which the coronavirus outbreak may impact our results is uncertain, it could result in delays in the manufacture of tenapanor, or in the delivery of key intermediates or raw materials required to manufacture tenapanor or delays in clinical development activities by us, or our collaboration partners. It could also materially and negatively impact our ability, either alone, or with a collaboration partner, to successfully commercialize tenapanor, if approved for marketing and sale by the FDA or foreign regulatory authorities, including our ability to educate physicians and patients about the benefits, administration and use of tenapanor.

- As a result of the COVID-19 pandemic, we may also experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- While our Phase 3 clinical development of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis is complete, we have ongoing and planned clinical trials for tenapanor and an ongoing Phase 2 clinical trial for RDX013, any of which may be delayed as a result the COVID-19 outbreak. Other potential impacts of the COVID-19 pandemic on our various clinical trials include delays or difficulties in any planned clinical site initiation, including difficulties in obtaining Institutional Review Board approvals, recruiting clinical site investigators and clinical site staff, delays or difficulties in enrolling patients, interruption of planned key clinical trial activities, such as clinical trial site data monitoring due to diversion of resources at clinical sites or limitation on travel imposed by federal or state governments.

- We have limited the use of our offices to essential employees and requested that most of our personnel, including all of our administrative employees, work remotely. We have restricted on-site staff to only those personnel and contractors who must perform essential activities that must be completed on-site and limited the number of staff in our research laboratories. The COVID-19 pandemic could disrupt our ability to secure supplies for our facilities and to provide personal protective equipment for our employees. The safety, health and well-being of our workforce is of primary concern and we may need to enact further precautionary measures to help minimize the risk of our employees being exposed to the novel coronavirus.

- Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. In addition, this could increase our cyber-security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, research or clinical trial sites and important agencies and contractors.

- The FDA and comparable foreign regulatory agencies may continue to experience operational interruptions or delays, which may impact timelines for regulatory submission, trial initiation and regulatory approval.

The COVID-19 outbreak continues to rapidly evolve. The extent to which the outbreak may impact our business, manufacturing, preclinical development activities, preclinical studies and planned clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of COVID-19, the duration of the outbreak, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

We may consider strategic transactions, such as acquisitions of companies, asset purchases, and/or in-licensing of products, product candidates or technologies. In addition, if we are unable to access capital on a timely basis and on terms that are acceptable to us, we may be forced to restructure certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the development or commercialization of tenapanor and/or the development of RDX013 or certain of our other product candidates through the use of alternative structures. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, spin outs, collaboration partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- up-front, milestone and royalty payments, equity investments and financial support of new research and development candidates including increase of personnel, all of which may be substantial;
- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities;
- higher-than-expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and could have a material adverse effect on our business, results of operations, financial condition and prospects.

If we seek and obtain approval to commercialize our product candidates outside of the United States, manufacture our product candidates outside of the United States, or otherwise engage in business outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

We or our collaboration partners may decide to seek marketing approval for certain of our product candidates outside the United States or otherwise engage in business outside the United States, including entering into contractual agreements with third-parties. We currently utilize contract manufacturing organizations located outside of the United States to manufacture our active drug substance for tenapanor. We are subject to additional risks related to entering these international business markets and relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing United States and foreign drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;

- different reimbursement systems, and different competitive drugs;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

Our business involves the use of hazardous materials and we and third-parties with whom we contract must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities involve the controlled storage, use and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and manufacturers and suppliers with whom we may contract are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. We cannot guarantee that the safety procedures utilized by third-party manufacturers and suppliers with whom we may contract will comply with the standards prescribed by laws and regulations or will eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage.

We may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

We have dual headquarters and one of our facilities is located in the San Francisco Bay Area, which in the past has experienced severe earthquakes. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our California facility, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Risks Related to Government Regulation

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country. Neither we nor any of our collaboration partners is permitted to market any drug product in the United States until we receive marketing approval from the FDA. Obtaining regulatory approval of a NDA can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable United States and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions or other actions, including:

- warning or untitled letters;
- civil and criminal penalties;
- injunctions;
- withdrawal of regulatory approval of products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending NDAs or supplements to approved NDAs.

Prior to obtaining approval to commercialize a drug candidate in the United States or abroad, we or our collaboration partners must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or other foreign regulatory agencies, that such drug candidates are safe and effective for their intended uses. The number of nonclinical studies and clinical trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our drug candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering drug candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a drug candidate for any or all targeted indications.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, typically takes many years following the commencement of clinical studies and depends upon numerous factors. The FDA and comparable foreign authorities have substantial discretion in the approval process and we may encounter matters with the FDA or such comparable authorities that requires us to expend additional time and resources and delay or prevent the approval of our product candidates. For example, the FDA may require us to conduct additional studies for a drug product either prior to or post-approval, such as additional drug-drug interaction studies or safety or efficacy studies, or it may object to elements of our clinical development program such as the number of subjects in our current clinical trials from the United States. Additionally, on April 29, 2021, the FDA determined that a submission we made in response to an information request from the FDA constituted a major amendment to our NDA for tenapanor for the control of serum phosphorus, resulting in a three-month extension of the PDUFA date to July 29, 2021. The FDA's information request included a request for additional analyses of our clinical data. The FDA may act on our application by either issuing an approval letter or a CRL. Should we wish to pursue our application after receiving a CRL, we may, if possible, resubmit the application with information that addresses the questions or issues identified by the FDA in order to support approval. Resubmissions are subject to review period targets, which vary depending on the underlying submission type and the content of the resubmission. The FDA's information request included a request for additional analyses of our clinical data. Finally, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or result in a decision not to approve an application for regulatory approval. Despite the time and expense exerted, failure can occur at any stage.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our, or our collaboration partners', clinical studies;

- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which approval is sought;

- the FDA or comparable foreign regulatory authorities may disagree with the interpretation of data from preclinical studies or clinical studies;

- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of a NDA or other submission or to obtain regulatory approval in the United States or elsewhere;

- we or our collaboration partners may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;

- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers responsible for clinical and commercial supplies; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical studies, may result in our failure and/or that of our collaboration partners to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects. Additionally, if the FDA requires that we conduct additional clinical studies, places limitations in our label, delays approval to market our product candidates or limits the use of our products, our business and results of operations may be harmed.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we receive regulatory approval for a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, any product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Even if a drug is approved by the FDA or foreign regulatory authorities, the manufacturing processes, labeling, packaging, distribution, pharmacovigilance, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCP regulations for any clinical trials that we conduct post-approval. As such, we and our third-party contract manufacturers will be subject to continual review and periodic inspections to assess compliance with regulatory requirements. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. Regulatory authorities may also impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-marketing studies. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs to assure compliance.

We will also be required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have FDA approval.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- warning or untitled letters, fines or holds on clinical trials;

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- injunctions or the imposition of civil or criminal penalties;
- suspension or revocation of existing regulatory approvals;
- suspension of any of our ongoing clinical trials;
- refusal to approve pending applications or supplements to approved applications submitted by us;
- restrictions on our or our contract manufacturers' operations; or
- product seizure or detention, or refusal to permit the import or export of products.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize our product candidates. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

In addition, the FDA's policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, the results of the 2020 President election may impact our business and industry. Namely, the Trump administration took several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict whether or how these Executive Orders will be implemented, or whether they will be rescinded or replaced under a Biden Administration. The policies and priorities of an incoming administration are unknown, and could materially impact the regulatory framework governing our products.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Separately, in response to the global COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most foreign inspections of manufacturing facilities and products through April 2020, and subsequently, on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020 the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other

policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.

All entities involved in the preparation of product candidates for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP regulations. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA or comparable regulatory filing on a timely basis and must adhere to cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent suspension of production or closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other applicable regulatory authority can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product, withdrawal of an approval, or suspension of production. As a result, our business, financial condition, and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through an NDA, a supplemental NDA or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical studies, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue.

If we fail to comply or are found to have failed to comply with FDA and other regulations related to the promotion of our products for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. If tenapanor or our other product candidates receive marketing

approval, we and our collaboration partners, if any, will be restricted from marketing the product outside of its approved labeling, also referred to as off-label promotion. However, physicians may nevertheless prescribe an approved product to their patients in a manner that is inconsistent with the approved label, which is an off-label use. We are implementing compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations regarding off-label promotion. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of our product candidates for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Over the past several years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the FFDCA, the False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "qui tam" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim, or caused a false claim to be submitted, to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

Tenapanor, which has been approved by the FDA for the treatment of IBS-C in adults, and/or RDX013, and our other product candidates, if approved, may cause or contribute to adverse medical events that we are required to report to regulatory agencies and if we fail to do so we could be subject to sanctions that would materially harm our business.

Some participants in clinical studies of tenapanor have reported adverse effects after being treated with tenapanor, including diarrhea, nausea, flatulence, abdominal discomfort, abdominal pain, abdominal distention and changes in electrolytes. If we are successful in commercializing any products, FDA and foreign regulatory agency regulations require that we report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the FDA or a foreign regulatory agency could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

Our employees, independent contractors, principal investigators, CROs, collaboration partners, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, collaboration partners, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate any of the following: FDA regulations, including those laws that require the reporting of true, complete and accurate financial and other information to the FDA; manufacturing standards; or federal and state healthcare fraud and abuse laws and regulations. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. These activities also include the improper use of information obtained in the course of clinical trials, which could

result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Failure to obtain regulatory approvals in foreign jurisdictions would prevent us from marketing our products internationally.

In order to market any product in the EEA (which is composed of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein), and many other foreign jurisdictions, separate regulatory approvals are required. In the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization ("MA"). Before the MA is granted, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

The approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not be able to file for regulatory approvals or to do so on a timely basis, and even if we do file we may not receive necessary approvals to commercialize our products in any market.

We and our collaboration partners may be subject to healthcare laws, regulation and enforcement; our failure or the failure of any such collaboration partners to comply with these laws could have a material adverse effect on our results of operations and financial conditions.

Although we do not currently have any products on the market, once we begin commercializing our products, we and our collaboration partners may be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. The laws that may affect our ability to operate as a commercial organization include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;

- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the false claims statutes;

- the federal Civil Monetary Penalties law, which prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary's decision to order or receive items or services reimbursable by the government from a particular provider or supplier;

- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation;

- the federal physician sunshine requirements under the ACA, which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to CMS information related to payments and other transfers of value to physicians,

certain other healthcare providers beginning in 2022, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers;

- state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources;

- state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or pricing information and marketing expenditures; and

- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to market our products and adversely impact our financial results.

Legislative or regulatory healthcare reforms in the United States may make it more difficult and costly for us to obtain regulatory clearance or approval of our product candidates and to produce, market and distribute our products after clearance or approval is obtained.

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the reimbursement thereof. In addition, FDA regulations and guidance are often revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of our product candidates. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;

- changes to manufacturing methods;

- recall, replacement, or discontinuance of one or more of our products; and

- additional record keeping.

Each of these would likely entail substantial time and cost and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any future products would harm our business, financial condition and results of operations.

In addition, the full impact of recent healthcare reform and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model. In the United States, the ACA was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The ACA, among other things, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-

sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. By way of example, the Tax Cuts and Jobs Act of 2017 included a provision repealing, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The Supreme Court heard argument on this case on November 10, 2020. On February 10, 2021, the Department of Justice notified the Court of the federal government's change in position from that presented in its brief on the merits filed in the case. It is unclear how the Supreme Court will rule. It is also unclear how other efforts, if any, to challenge, repeal, or replace the ACA will impact the ACA or our business. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect the demand for any drug products for which we may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These new laws, among other things, included aggregate reductions of Medicare payments of 2% per fiscal year to providers that will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through December 31, 2020, unless additional action is taken by Congress, additional specific reductions in Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and an increase in the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, individual states have become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and to encourage importation from other countries and bulk purchasing. Recently, there has also been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

Risks Related to Intellectual Property

We may become subject to claims alleging infringement of third parties' patents or proprietary rights and/or claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of tenapanor or our other product candidates, or prevent or delay the continued use of our drug discovery and development platform, including APECCS.

There have been many lawsuits and other proceedings asserting infringement or misappropriation of patents and other intellectual property rights in the pharmaceutical and biotechnology industries. There can be no assurances that we will not be subject to claims alleging that the manufacture, use or sale of tenapanor or any other product candidates, or that the use of our drug discovery and development platform, including APECCS, infringes existing or future third-party patents, or that such claims, if any, will not be successful. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of tenapanor or other product candidates or by the use of APECCS. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. We may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of tenapanor or our other product candidates, or by the use of APECCS.

We may be subject to third-party patent infringement claims in the future against us or our that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing a third party's patents. We may be required to indemnify future collaboration partners against such claims. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If a patent infringement suit were brought against us we

could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. In addition, if a patent infringement suit were brought against us regarding the use of aspects of our drug discovery and development platform, we could be forced to stop our use of APECCS or of other aspects of our platform, or we could be forced to modify our processes to avoid infringement, which may not be possible at a reasonable cost, if at all, and which could result in substantial delay in our use of our platform for the discovery of new product candidates or potential targets. As a result of patent infringement claims, or in order to avoid potential claims, we may choose to seek, or be required to seek, a license from the third party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, we may be unable to maintain such licenses and the rights may be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to cease our use of APECCS or some other aspect of our drug discovery and development platform or our business operations if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms, or unable to maintain such licenses when granted. Even if we are successful in defending against such claims, such litigation can be expensive and time consuming to litigate and would divert management's attention from our core business. Any of these events could harm our business significantly.

In addition to infringement claims against us, if third parties prepare and file patent applications in the United States that also claim technology similar or identical to ours, we may have to participate in interference or derivation proceedings in the United States Patent and Trademark Office (the "USPTO") to determine which party is entitled to a patent on the disputed invention. We may also become involved in similar opposition proceedings in the European Patent Office or similar offices in other jurisdictions regarding our intellectual property rights with respect to our products and technology. Since patent applications are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates.

If our intellectual property related to our product candidates is not adequate or if we are not able to protect our trade secrets or our confidential information, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates, our drug discovery and development platform and our development programs. Any disclosure to or misappropriation by third parties of our confidential or proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in foreign countries. Additionally, our research and development efforts may result in product candidates for which patent protection is limited or not available. Even if patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, U.S. patents can be challenged by any person before the new USPTO Patent Trial and Appeals Board at any time before one year after that person is served an infringement complaint based on the patents. Patents granted by the European Patent Office may be similarly opposed by any person within nine months from the publication of the grant. Similar proceedings are available in other jurisdictions, and in the United States, Europe and other jurisdictions third parties can raise questions of validity with a patent office even before a patent has granted. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. For example, a third party may develop a competitive product that provides therapeutic benefits similar to one or more of our product candidates but has a sufficiently different composition to fall outside the scope of our patent protection. If the breadth or strength of protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is successfully challenged, then our ability to commercialize such product candidates could be negatively affected, and we may face unexpected competition that could have a material adverse impact on our business. Further, if we encounter delays in our clinical trials, the period of time during which we or our collaboration partners could market tenapanor or other product candidates under patent protection would be reduced.

Even where laws provide protection, costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. If we or one of our collaboration partners were to initiate legal proceedings against a third party to enforce a patent covering the product candidate, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of

invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability against our intellectual property related to a product candidate, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business. Moreover, our competitors could counterclaim that we infringe their intellectual property, and some of our competitors have substantially greater intellectual property portfolios than we do.

We also rely on trade secret protection and confidentiality agreements to protect proprietary know-how that may not be patentable, processes for which patents may be difficult to obtain and/or enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology, to assign their inventions to us, and endeavor to execute confidentiality agreements with all such parties, we cannot be certain that we have executed such agreements with all parties who may have helped to develop our intellectual property or who had access to our proprietary information, nor can we be certain that our agreements will not be breached by such consultants, advisors or third parties, or by our former employees. The breach of such agreements by individuals or entities who are actively involved in the discovery and design of our potential drug candidates, or in the development of our discovery and design platform, including APECCS, could require us to pursue legal action to protect our trade secrets and confidential information, which would be expensive, and the outcome of which would be unpredictable. If we are not successful in prohibiting the continued breach of such agreements, our business could be negatively impacted. We cannot guarantee that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of marketing exclusivity for our product candidates, our business may be materially harmed.

Following the approval by the FDA for our NDA to market tenapanor for IBS-C, we became eligible to seek and sought patent term restoration under the Hatch-Waxman Act for one of the U.S. patents covering our approved product or the use thereof. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product. Patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Despite seeking patent term extension for tenapanor or other product candidates, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions to maintain patent applications and issued patents. Noncompliance with these requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

We may not be able to enforce our intellectual property rights throughout the world.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain and enforce adequate intellectual property protection for our technology.

We may be subject to claims that we or our employees have misappropriated the intellectual property, including know-how or trade secrets, of a third party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at or engaged by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, consultants and contractors, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees, consultants and contractors do not use the intellectual property and other proprietary information or know-how or trade secrets of others in their work for us, and do not perform work for us that is in conflict with their obligations to another employer or any other entity, we may be subject to claims that we or these employees, consultants and contractors have used or disclosed such intellectual property, including know-how, trade secrets or other proprietary information. In addition, an employee, advisor or consultant who performs work for us may have obligations to a third party that are in conflict with their obligations to us, and as a result such third party may claim an ownership interest in the intellectual property arising out of work performed for us. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, or access to consultants and contractors. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

Risks Related to Our Common Stock

Our stock price may be volatile and our stockholders may not be able to resell shares of our common stock at or above the price they paid.

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include those discussed in this “Risk Factors” section and others such as:

- announcements of regulatory decisions regarding our NDA seeking marketing approval for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication;

- results of regulatory inspections of our facilities or those of our contract manufacturing organizations, or specific label restrictions or patient populations for tenapanor’s use, or changes or delays in the regulatory review process;

- announcements regarding whether tenapanor, alone or with other oral only medications, will be included in the bundled prospective payment system for the treatment of ESRD patients, and the time and manner in which such transition is achieved;
- results from, or any delays in, our RDX013 Phase 2 clinical trial;
- announcements relating to our current or future collaboration partnerships;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our product label, our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to our approved products or our product candidates;
- the success of our testing and clinical trials;
- failure to meet any of our projected timelines or goals with regard to the clinical development and commercialization of any of our product candidates;
- the success of our efforts to acquire or license or discover additional product candidates;
- any intellectual property infringement actions in which we may become involved;
- the success of our efforts to obtain adequate intellectual property protection for our product candidates;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry or other healthcare reform measures in the United States;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of our common stock;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- sales of debt securities and sales or licensing of assets;
- general economic and market conditions and overall fluctuations in the United States equity markets; and
- the loss of any of our key scientific or management personnel.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

Our principal stockholders own a significant percentage of our stock and, together with our management, will be able to exert significant control over matters subject to stockholder approval.

Based on the number of shares outstanding as of March 31, 2021, our officers, directors and stockholders who hold at least 5% of our stock together beneficially own approximately 40.8% of our outstanding common stock. If these officers, directors, and principal stockholders or a group of our principal stockholders act together, they will be able to exert a significant degree of influence over our management and affairs and control matters requiring stockholder approval, including the election of directors, amendments to our organizational documents, and approval of any merger, sale of assets or other business combination transactions. The interests of this concentration of ownership may not always coincide with our interests or the interests of other stockholders. For instance, officers, directors and principal stockholders, acting together, could cause us to enter into transactions or agreements that we would not otherwise consider. Similarly, this concentration of ownership may have the effect of delaying or preventing a change in control of our company otherwise favored by our other stockholders.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of March 31, 2021, we had approximately 98.7 million shares of common stock outstanding. Of those shares, approximately 37.4 million were held by current directors, executive officers and stockholders owning 5% or more of our outstanding common stock.

As of March 31, 2021, 1.0 million shares of common stock issuable upon vesting of outstanding restricted stock units and approximately 12.3 million shares of common stock issuable upon exercise of outstanding options were eligible for sale in the public market to the extent permitted by the provisions of the applicable vesting schedules, and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are issued and sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

General Risk Factors

We incur significant costs as a result of operating as a public company, and our management will devote substantial time to new compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business.

We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Securities Exchange Act of 1934, as amended (the “Exchange Act”) and regulations regarding corporate governance practices. The listing requirements of The Nasdaq Global Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors’ and officers’ insurance, on acceptable terms.

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002 (“Section 404”) and the related rules of the Securities and Exchange Commission (“SEC”) which require, among other things, our management to report on the effectiveness of our internal control over financial reporting. Our compliance with Section 404 requires that we incur substantial expense and expend significant management efforts.

During the course of our review and testing of our internal controls, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The Nasdaq Global Market or other adverse consequences that would materially harm our business.

We may be adversely affected by the global economic environment.

Our ability to attract and retain collaboration partners or customers, invest in and grow our business and meet our financial obligations depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States, presidential elections, other political influences and inflationary pressures. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The 2008 global financial crisis caused extreme volatility and disruptions in the capital and credit markets. We cannot anticipate all the ways in which the global economic climate and global financial market conditions could adversely impact our business in the future.

We are exposed to risks associated with reduced profitability and the potential financial instability of our collaboration partners or customers, many of which may be adversely affected by volatile conditions in the financial markets. For example, unemployment and underemployment, and the resultant loss of insurance, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, our collaboration partners or customers may experience reductions in revenues, profitability and/or cash flow that could lead them to reduce their support of our programs or financing activities. If collaboration partners or customers are not successful in generating sufficient revenue or are precluded from securing financing, they may not be able to pay, or may delay payment of, accounts receivable that are owed to us. In addition, volatility in the financial markets could cause significant fluctuations in the interest rate and currency markets. We currently do not hedge for these risks. The foregoing events, in turn, could adversely affect our financial condition and liquidity. In addition, if economic challenges in the United States result in widespread and prolonged unemployment, either regionally or on a national basis, or if certain provisions of the Patient Protection and ACA, as amended by the Health Care and Education Reconciliation Act, collectively known as the ACA, are repealed, a substantial number of people may become uninsured or underinsured. To the extent economic challenges result in fewer individuals pursuing or being able to afford our product candidates once commercialized, our business, results of operations, financial condition and cash flows could be adversely affected.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquirer or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least two-thirds of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;

- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;

- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;

- the required approval of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;

- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;

- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and

- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.

- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.

- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.

- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.

- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Additionally, the terms of our loan and security agreements could restrict our ability to pay dividends. Therefore, our stockholders are not likely to receive any dividends on our common stock for the foreseeable future. Since we do not intend to pay dividends, our stockholders' ability to receive a return on their investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business.

Following a national referendum and enactment of legislation by the government of the United Kingdom, the United Kingdom formally withdrew from the European Union and ratified a trade and cooperation agreement governing its future relationship with the European Union. The agreement, which is being applied provisionally from January 1, 2021 until it is ratified by the European Parliament and the Council of the European Union, addresses trade, economic arrangements, law enforcement, judicial cooperation and a governance framework including procedures for dispute resolution, among other things. Because the agreement merely sets forth a framework in many respects and will require complex additional bilateral negotiations between the United Kingdom and the European Union as both parties continue to work on the rules for implementation, significant political and economic uncertainty remains about how the precise terms of the relationship between the parties will differ from the terms before withdrawal.

These developments, or the perception that any related developments could occur, have had and may continue to have a material adverse effect on global economic conditions and financial markets, and may significantly reduce global market liquidity, restrict the ability of key market participants to operate in certain financial markets or restrict our access to capital. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and reduce the price of our common stock.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Effective May 16, 2018, we entered into a loan and security agreement (as amended on October 9, 2020) pursuant to which the Lenders agreed to provide us a $50.0 million term loan facility. Covenants in the loan and security agreement limit our ability to pay dividends or make other distributions. For additional information refer to "NOTE 5. BORROWINGS" in the notes to our unaudited condensed financial statements in Part I, Item 1, *Notes to Condensed Financial Statements*, of this Quarterly Report on Form 10-Q.

Unregistered Sales of Equity Securities

None.

Use of Proceeds

Not applicable.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

(a) None.

ITEM 6. Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.1	Third Amendment to the Loan and Security Agreement, dated May 5, 2021, by and between the Company and Solar Capital Ltd. and Western Alliance Bank.				X
31.1	Certification of Chief Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of Chief Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1	Certification of Chief Executive Officer and Chief Financial Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
101	The following financial statements, formatted in Inline Extensible Business Reporting Language (XBRL): (i) Condensed Balance Sheets as of March 31, 2021 and December 31, 2020, (ii) Condensed Statements of Operations and Comprehensive Loss for the three months ended March 31, 2021 and 2020, (iii) Condensed Statements of Cash Flows for the nine months ended March 31, 2021 and 2020, and (iv) Notes to Unaudited Condensed Financial Statements.				X
104	Cover Page Interactive Data File, formatted in Inline XBRL and contained in Exhibit 101.				

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Ardelyx, Inc.

Date: May 6, 2021

By: /s/ Justin Renz

Justin Renz
Chief Financial Officer
(Chief Accounting and Principal Financial Officer)

THIRD AMENDMENT TO LOAN AND SECURITY AGREEMENT

THIS **THIRD AMENDMENT TO LOAN AND SECURITY AGREEMENT** (this "**Amendment**"), dated as of May 5, 2021 (the "**Amendment Effective Date**"), is made by and among Ardelyx, Inc., a Delaware corporation ("**Borrower**"), SLR Investment Corp., a Maryland corporation and formerly known as Solar Capital Ltd. ("**Solar**"), in its capacity as collateral agent for Lenders (in such capacity, together with its successors and assigns in such capacity, "**Collateral Agent**"), and the Lenders listed on Schedule 1.1 of the Loan and Security Agreement (as defined below) or otherwise a party hereto from time to time including Solar in its capacity as a Lender and Western Alliance Bank, an Arizona corporation, as a Lender (each a "**Lender**" and collectively, the "**Lenders**").

The Borrower, the Lenders and Collateral Agent are parties to a Loan and Security Agreement dated as of May 16, 2018 (as amended, restated or modified from time to time, including by that certain First Amendment to Loan and Security Agreement, dated as of October 9, 2020, and that certain Second Amendment to Loan and Security Agreement, dated as of March 1, 2021, the "**Loan and Security Agreement**"). The Borrower has requested that the Lenders agree to certain amendments to the Loan and Security Agreement. The Lenders have agreed to such request, subject to the terms and conditions hereof.

Accordingly, the parties hereto agree as follows:

SECTION 1. Definitions; Interpretation.

(a) **Terms Defined in Loan and Security Agreement**. All capitalized terms used in this Amendment (including in the recitals hereof) and not otherwise defined herein shall have the meanings assigned to them in the Loan and Security Agreement.

(b) **Interpretation**. The rules of interpretation set forth in Section 1.1 of the Loan and Security Agreement shall be applicable to this Amendment and are incorporated herein by this reference.

SECTION 2. Amendments to the Loan and Security Agreement.

(a) The Loan and Security Agreement shall be amended as follows effective as of the Amendment Effective Date:

(i)Section 2.2(b)(ii) of the Loan and Security Agreement is amended and restated as follows:

"(ii) Commencing on the Amortization Date, and continuing on the Payment Date of each month thereafter, Borrower shall (i) make monthly payments of interest to the respective Lender to which such payments are owed in accordance with their respective Pro Rata Shares, as calculated by Collateral Agent (which calculations shall be deemed correct absent manifest error) based upon the effective rate of interest applicable to the Term Loan, as determined in Section 2.3(a) plus (ii) make consecutive equal monthly payments of principal to the respective Lender to which such payments are owed in accordance with their respective Pro Rata Shares, as calculated by Collateral Agent (which calculations shall be deemed correct absent manifest error) based upon: (A) the respective principal amounts of such Lender's Term Loan outstanding less the additional principal payment (if any) pursuant to the proviso at the end of this sentence, and (B) a repayment schedule equal to the number of months from (and including) the

Amortization Date through (and including) the Maturity Date; provided, however, (1) if the Amortization date is July 1, 2021, Borrower shall make an additional principal payment to Lenders on such date in an amount equal to $2,777,777.78 and (2) if the Amortization Date is August 1, 2021, Borrower shall make an additional principal payment to Lenders on such date in an amount equal to $5,555,555.55, in either case, without any Prepayment Premium in respect of such additional principal payment. All unpaid principal and accrued and unpaid interest with respect to each such Term Loan is due and payable in full on the Maturity Date. The Term Loan may only be prepaid in accordance with Sections 2.2(c) and 2.2(d)."

(ii)The defined term "Amortization Date" is hereby amended and restated in its entirety as follows:

"**Amortization Date**" means December 1, 2021; provided, however, if either (a) the FDA does not approve the Borrower's New Drug Application for tenapanor for control of serum phosphorus in adult chronic kidney disease patients (CKD) on dialysis on or before July 31, 2021 or (b) the FDA issues a complete response letter ("CRL") for tenapanor for the control of serum phosphorus in adult chronic kidney disease patients (CKD) on dialysis, in each case, subject to reasonable verification by Collateral Agent (including supporting documentation reasonably requested by Collateral Agent), then the Amortization Date shall mean the earlier of (x) August 1, 2021, or (y) the first (1st) day of the month immediately following the date that the FDA issues a CRL to Borrower.

(b) **References Within Loan and Security Agreement**. Each reference in the Loan and Security Agreement to "this Agreement" and the words "hereof," "herein," "hereunder," or words of like import, shall mean and be a reference to the Loan and Security Agreement as amended by this Amendment.

SECTION 3. Conditions of Effectiveness. The effectiveness of Section 2 of this Amendment shall be subject to the satisfaction of each of the following conditions precedent:

(a) **Fees and Expenses**. The Borrower shall have paid (i) an amendment fee of Twenty-Five Thousand Dollars ($25,000) to be shared between the Lenders seventy percent (70%) to Solar and thirty percent (30%) to Western Alliance Bank, and (ii) all invoiced costs and expenses then due in accordance with Section 5(e).

(b) **This Amendment**. Collateral Agent shall have received this Amendment, executed by Collateral Agent, the Lenders and the Borrower.

(c) **Representations and Warranties; No Default**. On the Amendment Effective Date, after giving effect to the amendment of the Loan and Security Agreement contemplated hereby:

(i)The representations and warranties contained in Section 4 shall be true and correct in all material respects on and as of the Amendment Effective Date as though made on and as of such date; and

(ii)There exist no Events of Default.

SECTION 4. Representations and Warranties. To induce the Lenders to enter into this Amendment, the Borrower hereby confirms, as of the date hereof, (a) that the representations and warranties made by it in Section 5 of the Loan and Security Agreement and in the other Loan Documents are true and correct in

all material respects; *provided*, *however*, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; (b) that there has not been and there does not exist a Material Adverse Change; and (c) that the information included in the Perfection Certificate most recently delivered to Collateral Agent pursuant to Section 6.2(a)(xiv) of the Loan Agreement remains true and correct in all material respects. For the purposes of this Section 4, (i) each reference in Section 5 of the Loan and Security Agreement to "this Agreement," and the words "hereof," "herein," "hereunder," or words of like import in such Section, shall mean and be a reference to the Loan and Security Agreement as amended by this Amendment, and (ii) any representations and warranties which relate solely to an earlier date shall not be deemed confirmed and restated as of the date hereof (provided that such representations and warranties shall be true, correct and complete in all material respects as of such earlier date).

SECTION 5. Miscellaneous.

(a) **Loan Documents Otherwise Not Affected; Reaffirmation**. Except as expressly amended pursuant hereto or referenced herein, the Loan and Security Agreement and the other Loan Documents shall remain unchanged and in full force and effect and are hereby ratified and confirmed in all respects. The Lenders' and Collateral Agent's execution and delivery of, or acceptance of, this Amendment shall not be deemed to create a course of dealing or otherwise create any express or implied duty by any of them to provide any other or further amendments, consents or waivers in the future. The Borrower hereby reaffirms the grant of security under Section 4.1 of the Loan and Security Agreement and hereby reaffirms that such grant of security in the Collateral secures all Obligations under the Loan and Security Agreement, including without limitation any Term Loans funded on or after the Amendment Effective Date, as of the date hereof.

(b) **Conditions**. For purposes of determining compliance with the conditions specified in Section 3, each Lender that has signed this Amendment shall be deemed to have consented to, approved or accepted or to be satisfied with, each document or other matter required thereunder to be consented to or approved by or acceptable or satisfactory to a Lender unless Collateral Agent shall have received notice from such Lender prior to the Amendment Effective Date specifying its objection thereto.

(c) **Release**. In consideration of the agreements of Collateral Agent and each Lender contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Borrower, on behalf of itself and its successors, assigns, and other legal representatives, hereby fully, absolutely, unconditionally and irrevocably releases, remises and forever discharges Collateral Agent and each Lender, and its successors and assigns, and its present and former shareholders, affiliates, subsidiaries, divisions, predecessors, directors, officers, attorneys, employees, agents and other representatives (Collateral Agent, Lenders and all such other persons being hereinafter referred to collectively as the "**Releasees**" and individually as a "**Releasee**"), of and from all demands, actions, causes of action, suits, covenants, contracts, controversies, agreements, promises, sums of money, accounts, bills, reckonings, damages and any and all other claims, counterclaims, defenses, rights of set-off, demands and liabilities whatsoever of every name and nature, known or unknown, suspected or unsuspected, both at law and in equity, which Borrower, or any of its successors, assigns, or other legal representatives may now or hereafter own, hold, have or claim to have against the Releasees or any of them for, upon, or by reason of any circumstance, action, cause or thing whatsoever which arises at any time on or prior to the day and date of this Amendment, including, without limitation, for or on account of, or in relation to, or in any way in connection with the Loan Agreement, or any of the other Loan Documents or transactions thereunder or related thereto. Borrower understands, acknowledges and agrees that the release set forth above may be pleaded as a full and complete defense and may be used as a basis

for an injunction against any action, suit or other proceeding which may be instituted, prosecuted or attempted in breach of the provisions of such release. Borrower agrees that no fact, event, circumstance, evidence or transaction which could now be asserted or which may hereafter be discovered shall affect in any manner the final, absolute and unconditional nature of the release set forth above.

(d) **No Reliance**. The Borrower hereby acknowledges and confirms to Collateral Agent and the Lenders that the Borrower is executing this Amendment on the basis of its own investigation and for its own reasons without reliance upon any agreement, representation, understanding or communication by or on behalf of any other Person.

(e) **Costs and Expenses**. The Borrower agrees to pay to Collateral Agent within the later of (i) ten (10) days following its receipt of an invoice, or (ii) ten (10) days following the Amendment Effective Date, the reasonable and documented out-of-pocket costs and expenses of Collateral Agent and the Lenders party hereto, and the reasonable and documented fees of counsel to Collateral Agent and the Lenders party thereto, in connection with the negotiation, preparation, execution and delivery of this Amendment and any other documents to be delivered in connection herewith on the Amendment Effective Date.

(f) **Binding Effect**. This Amendment binds and is for the benefit of the successors and permitted assigns of each party.

(g) **Governing Law**. **THIS AMENDMENT AND THE RIGHTS AND OBLIGATIONS OF THE PARTIES HEREUNDER SHALL IN ALL RESPECTS BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH, THE INTERNAL LAWS OF THE STATE OF NEW YORK (WITHOUT REGARD TO THE CONFLICT OF LAWS PRINCIPLES THAT WOULD RESULT IN THE APPLICATION OF ANY LAWS OTHER THAN THE LAWS OF THE STATE OF NEW YORK (OTHER THAN SECTION 5-1401 OF THE GENERAL OBLIGATIONS LAW)), INCLUDING ALL MATTERS OF CONSTRUCTION, VALIDITY AND PERFORMANCE, REGARDLESS OF THE LOCATION OF THE COLLATERAL.**

(h) **Complete Agreement; Amendments; Exit Fee Agreement**. This Amendment and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements with respect to such subject matter. All prior agreements, understandings, representations, warranties, and negotiations between the parties about the subject matter of this Amendment and the Loan Documents merge into this Amendment and the Loan Documents. For the avoidance of doubt and notwithstanding anything to the contrary in this Amendment, Borrower (a) reaffirms its obligations under the Exit Fee Agreement, including without limitation its obligation to pay the Exit Fee (as defined in the Exit Fee Agreement) if and when due thereunder, and (b) agrees that the defined term "Loan Agreement" as defined in the Exit Fee Agreement shall on and after the Amendment Effective Date mean the Loan and Security Agreement as amended by this Amendment and may be amended, restated or modified from time to time on or after the Amendment Effective Date.

(i) **Severability of Provisions.** Each provision of this Amendment is severable from every other provision in determining the enforceability of any provision.

(j) **Counterparts**. This Amendment may be executed in any number of counterparts and by different parties on separate counterparts, each of which, when executed and delivered, is an original, and all taken together, constitute one Amendment. Delivery of an executed counterpart of a signature page of

this Amendment by facsimile, portable document format (.pdf) or other electronic transmission will be as effective as delivery of a manually executed counterpart hereof.

(k) **Loan Documents**. This Amendment and the documents related thereto shall constitute Loan Documents

(l) **Electronic Execution of Certain Other Documents**. The words "execution," "execute", "signed," "signature," and words of like import in or related to any document to be signed in connection with this Amendment and the transactions contemplated hereby (including without limitation assignments, assumptions, amendments, waivers and consents) shall be deemed to include electronic signatures, the electronic matching of assignment terms and contract formations on electronic platforms approved by Collateral Agent, or the keeping of records in electronic form, each of which shall be of the same legal effect, validity or enforceability as a manually executed signature or the use of a paper-based recordkeeping system, as the case may be, to the extent and as provided for in any applicable law, including the Federal Electronic Signatures in Global and National Commerce Act, the New York State Electronic Signatures and Records Act, or any other similar state laws based on the Uniform Electronic Transactions Act.

[Balance of Page Intentionally Left Blank; Signature Pages Follow]

IN WITNESS WHEREOF, the parties hereto have duly executed this Amendment, as of the date first above written.

BORROWER:

ARDELYX, INC.,
as Borrower
By: /s/ Justin Renz
Name: Justin Renz
Title: Chief Financial Officer

COLLATERAL AGENT AND LENDER:

SLR INVESTMENT CORP.,
as Collateral Agent and a Lender

By: /s/ Anthony J. Storino
Name: Anthony J. Storino
Title: Authorized Signatory

LENDER:

SCP PRIVATE CREDIT INCOME FUND SPV, LLC,
as a Lender

By: /s/ Anthony J. Storino
Name: Anthony J. Storino
Title: Authorized Signatory

LENDER:

WESTERN ALLIANCE BANK,
as a Lender

By: //s/ Bill Wickline
Name: Bill Wickline
Title: Head of Life Sciences

Exhibit 31.1

CERTIFICATION

I, Michael Raab, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ardelyx, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 6, 2021

By: /s/ Michael Raab

Michael Raab
President Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Justin Renz, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ardelyx, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 6, 2021

By: /s/ Justin Renz

Justin Renz
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of Ardelyx, Inc. (the "Company") on Form 10-Q for the period ending March 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Michael Raab, President and Chief Executive Officer of the Company, and Justin Renz, Chief Financial Officer of the Company, respectively, do each hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: May 6, 2021 By: /s/ Michael Raab

Michael Raab
President Chief Executive Officer and Director
(Principal Executive Officer)

Date: May 6, 2021 By: /s/ Justin Renz

Justin Renz
Chief Financial Officer
(Principal Financial and Accounting Officer)